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It is the aim of this journal to provide the reader with abstracts of all important articles appearing in medical periodicals published in every part of the world, and in this way to enable him to keep in touch with new developments throughout the whole field of medicine and in each of its special branches, including those aspects of surgery which are of particular concern to the physician.

More than 1,600 periodicals are surveyed, from which are selected for abstracting those papers which appear to make some useful contribution to the sum of medical knowledge or experience. Each paper is abstracted in sufficient detail to indicate to the general reader the nature and value of that contribution and to enable the specialist to assess its importance in relation to his own work and to decide whether the original article should be read in full. The author's own summary or an editorial summary published with the original article may occasionally be reproduced if it is suitable for these purposes, and the title and reference alone may be published in order to draw attention to a review article or other type of paper which cannot readily be abstracted.

The abstracts in each issue are grouped in sections according to subject and, so far as possible, those dealing with medical and surgical aspects of the same problem appear together. The titles of papers written in languages other than English are given both in translation and in the original form. The titles of journals are given in full and also abbreviated according to the rules adopted in the *World List of Scientific Periodicals*, as modified by *ISO Recommendation R4: International Code for the Abbreviation of Titles of Periodicals* (International Standards Organization, 1957), and in *World Medical Periodicals* (Second Edition, World Medical Association, 1957). The transliteration of authors' names from the Cyrillic alphabets is in accordance with *ISO Recommendation R9: International System for the Transliteration of Cyrillic Characters* (International Standards Organization, 1955).

Explanatory or critical comments by the abstracter or editor are enclosed within square brackets.

ABSTRACTS OF WORLD MEDICINE

VOL. 29 NO. 3 MARCH, 1961

Pathology

417. **The Trypsin Inhibitor Capacity of Serums in Normal and Diseased States**

G. M. HOMER, R. E. ZIPF, T. E. HIEBER, and B. J. KATCHMAN. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **34**, 99–107, Aug. [received Oct.], 1960. 3 figs., 23 refs.

Human serum has an inhibitory effect on the activity of trypsin, and elevated values for serum trypsin inhibitor (S.T.I.) may be clinically significant in the diagnosis of several disease states. At Miami Valley Hospital, Dayton, Ohio, serum trypsin inhibitor capacity was determined, casein labelled with radioactive iodine being used as substrate. In 103 healthy subjects the mean S.T.I. capacity was found to be 0·87 (S.D. 0·14) mg. of trypsin inhibited per ml. of serum. Raised values were found in 13 out of 17 patients with pancreatic disease (pancreatitis, cystic fibrosis, or neoplasm) and in 8 out of 58 patients with diseases not affecting the pancreas; low values were observed in 2 patients in the latter group. The authors suggest that estimation of the S.T.I. capacity may be of value in the diagnosis of pancreatic disease and also in assessing the efficacy of treatment.

M. Lubran

EXPERIMENTAL PATHOLOGY

418. **Development of Heat Pyrexia**

J. GOLD. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **173**, 1175–1182, July 16, 1960. 7 figs., 14 refs.

It has been noted that the cardiovascular system appears to take the brunt of exposure to heat, peripheral venous pressure being constantly increased even when the subject is standing or sitting erect. It was therefore decided to investigate the part that the cardiovascular system plays in the syndrome of heat pyrexia. Healthy subjects aged between 20 and 50 were exposed to a temperature of 54·5° C. (130° F.) for 2 hours or one of 71° C. (160° F.) for one hour at a vapour pressure of 10 mm. Hg (relative humidity 8% and 4% respectively). Calculation (by Burton's method) of the effective body heat storage under these conditions revealed that this was nearly twice as high in the oldest subjects as in the youngest subjects (16·5 and 8·5 Cal. per sq. metre body surface per hour respectively). Heat dissipation tests, in which the subjects drank one litre of iced water during this period, demonstrated that younger subjects can make better use of this cooling mechanism than older. Direct measurements of the venous pressure showed that it rose in direct relationship with effective body heat storage.

In one subject exposed to various temperatures and vapour pressures, after the absorption of 82 effective Calories the venous pressure was increased to over 5 times its initial value, the subject being then near heat collapse. The effect on the cardiac output was also determined in one subject. At rest the output was 10·6 litres a minute, but after 75 effective Calories had been absorbed it rose to 16·9 litres per minute; thereafter signs of heat stroke set in and the cardiac output fell to 6·4 litres a minute. Estimation of the blood oxygen level at this time showed that the arterio-venous difference had fallen from an initial value of 3·9 vol.% to 1·6 vol.%, whereas the carbon dioxide A–V difference rose from 2·4 vol.% to 11·8 vol.%. These findings corresponded with the clinical appearance of the subjects approaching heat exhaustion. From radiographic studies it was found that the size of the cardiac shadow decreased during exposure to heat, presumably as a result of an extravascular shift of blood. Haemic murmurs also developed during the experiment. In younger subjects there was a fall in diastolic pressure, which during severe exposure occasionally progressed to zero, whereas in older subjects, if there was an increased pulse pressure, it was most frequently at the expense of an increase in the systolic pressure—a physiologically deleterious event. It was also found that the osmotic pressure of the plasma increased slightly during heat exposure.

From these findings and an analysis of the men's subjective impressions obtained during exposure to heat a possible mechanism of the circulatory collapse in heat pyrexia is suggested. It is considered that the primary pathology in heat stroke which finally brings about circulatory collapse is a high-output type of cardiac failure, the mechanism being as follows. The greatly diminished peripheral resistance allows for an abundantly increased and rapid venous return, which in turn increases the cardiac output. The left side of the heart cannot keep pace with the right so that this increase in venous return results in elevation of venous pressure. This increase in venous pressure also causes cessation of sweating. As the pressure increases the sweat rate begins to fall, but as the patient recovers and the venous pressure decreases sweating starts again. This sequence of events in heat exhaustion explains why older subjects are more prone to heat stroke than younger subjects, their normal compensatory mechanisms being far less efficient. It is therefore suggested that in the treatment of collapse in

heat stroke administration of fluids intravenously in combination with digitalization may well be an effective adjuvant to the usual methods of body cooling.

R. F. Jennison

419. **The Vascularized Cardiac Thrombus as a Possible Vicarious Source of Blood Supply in Ischemic Human Hearts**

F. L. RODRIGUEZ, S. L. ROBBINS, and G. K. MALLORY. *American Heart Journal* [*Amer. Heart J.*] **60**, 168–178, Aug., 1960. 9 figs., 6 refs.

It is possible that vessels formed in mural thrombi may convey blood from the lumen of the heart to the myocardium. At the City Hospital and Harvard Medical School, Boston, the hearts of 100 patients who had had coronary thrombosis with infarction of the left ventricle were examined histologically and the presence or absence of vascular intercommunications between the lumen of the left ventricle, the thrombus, and the myocardium was determined. An occasional endothelialized channel leading from the free surface of the thrombus into its substance was demonstrated in sections from 31 hearts. In sections from 42 hearts a communication was observed between the vessels of the thrombus and those of the myocardium; in 9 of the specimens both forms of communication were present, but there was no evidence of continuity between them.

A radio-opaque mass, consisting of barium sulphate and gelatin, was injected into the coronary system in 8 other hearts, penetrating to vessels as small as 40 μ in diameter. In 5 of these hearts the barium sulphate crossed from the coronary circulation to the cardiac lumen. All the injected vessels were lined with endothelium and there was no extravasation into the myocardium or the thrombus. The leakage could be seen to have occurred in the area of healed infarction bearing a thrombus. The barium sulphate failed to pass the infarcted zone adjacent to the thrombus in the remaining 3 hearts. Vascular openings on the surface of the thrombus and vascular bridges to the myocardium were demonstrated histologically. A further 4 hearts were injected through the coronary system as before and also injected with indian ink under pressure into the left ventricle through the mitral and aortic openings. In 2 of these the indian ink passed from the lumen of the heart through the vessels of the thrombus into the vessels of the myocardium. In the other 2 the barium sulphate had leaked into the cardiac lumen, but the ink had penetrated only as far as the thrombus.

Of the 9 hearts in which complete intercommunication was demonstrated, 7 contained old and 2 contained recent thrombi. The intercommunications appeared to be larger in the older thrombi (the largest here being 400 μ in diameter) than in the new. The barium sulphate failed to penetrate to the cardiac lumen in the 2 hearts with recent thrombi.

In the authors' view the evidence indicates that " in infarcted human hearts with cardiac thrombi vascular communications may form between the lumen of the left ventricle, the vessels of the organizing thrombus, and the coronary system . . . these communications may persist in old thrombi and can be of substantial size ". They state that investigations to define how these communications form and what the conditions are for their occurrence, persistence, and enlargement are in progress.

G. Clayton

420. **Measurement of Coronary Artery Blood-flow following Experimental Ligation of the Internal Mammary Artery**

C. R. BLAIR, R. F. ROTH, and H. A. ZINTEL. *Annals of Surgery* [*Ann. Surg.*] **152**, 325–329, Aug., 1960. 2 figs., 8 refs.

Two separate studies utilizing the same experimental procedure and designed to measure changes in coronary flow following bilateral internal mammary artery ligation are now reported. The conclusion is that in the majority of dogs there is a small additional blood flow (5·5 to 9·6 c.c. per minute) from the extra-cardiac mammary circulation to the coronary circulation.—[Authors' summary.]

421. **The Toxic Properties of Massive Inoculums of Newcastle Disease Virus and Influenza Virus (PR8) for Cell Strains Derived from Normal and Neoplastic Tissue**

E. J. MASON and N. KAUFMAN. *American Journal of Pathology* [*Amer. J. Path.*] **37**, 231–243, Aug., 1960. 5 figs., 18 refs.

It has been shown that Newcastle disease virus and influenza virus (strain PR8) have a toxic effect on some cell strains of human origin. In this paper from Western Reserve University School of Medicine, Cleveland, Ohio, the authors describe experiments designed to determine the action of these two viruses, in the form of infected allantoic fluid, on 5 cell strains, both normal and neoplastic, from human and murine sources. If the concentration of virus in the inoculum represented a virus to cell ratio greater than 10:1 a cytotoxic effect was produced. Lower ratios were without effect. Both viruses exerted approximately the same degree of cytopathogenicity for each of the cell strains. *H. Harris*

422. **The Influence of Cortisone on the Course of Viral Infections.** (Zur Beeinflussung des Virusinfektes durch Cortison)

E. WASIELEWSKI, B. KNICK, and W. BÜNNAGEL. *Zentralblatt für Bakteriologie, Parasitenkunde, Infektionskrankheiten und Hygiene* [*Zbl. Bakt., I. Abt. Orig.*] **179**, 437–447, 1960. Bibliography.

The multiplication of virus in cells is influenced by the metabolism of the cells, and the latter can be influenced by certain hormones, such as cortisone-like substances. It has frequently been noted that in the presence of cortisone the course of a virus infection is changed and usually considerably worsened, depending on whether the cortisone was administered before or after the onset of the infection. At the University of Mainz the present investigations were carried out on groups of mice infected with the viruses of mumps encephalitis, herpes, and influenza A and B. The mortality among cortisone-treated animals was significantly higher than that among the controls. In apparent contradiction to this finding, however, the number of demonstrable " infectious units

per weight of tissue " was smaller in the animals treated with cortisone.

The authors suggest that the action of cortisone takes place in two phases—namely, an initial inhibition of the virus and later acceleration of virus multiplication. The first phase would explain the relatively lower number of infectious units. In addition, a decrease in the defences of the host appears to be responsible for the simultaneous worsening of the clinical course of the infection. *E. Forrai*

423. **Differential Analysis of the Stages of Hepatic Excretory Function with Gamma Emitting Isotopes. I. Methods and Validation**

E. ENGLERT JR., B. A. BURROWS, and F. J. INGELFINGER. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **56**, 181–192, Aug., 1960. 5 figs., 20 refs.

Anionic phthalein dyes, such as rose bengal, are removed from the plasma by the liver and are excreted in the bile. At Boston University School of Medicine, a gamma-ray-emitting isotope of iodine (^{131}I) was substituted for the iodine in the rose bengal molecule and the radioiodinated dye (R.I.R.B.) was followed by a sensitive radiation detector during its excretion by the liver. Physical variables such as the size of the patient, the distance between the radiation source and the counter, and the differential tissue densities were evaluated. Another factor considered was the effect on the detector of radioactivity from dye circulating through the liver and from excreted dye in the gall-bladder and small intestine. The readings for the uptake and excretion were correlated with the results of other hepatic excretion function tests and efforts were made to reproduce the results obtained. Material and methods are adequately described, with particular details of a directional detector which rejects back scatter outside a small collimated area. The position of the detector while taking readings was found to be critical. Hepatic radioactivity was recorded after intravenous injection of 5 to 10 μc. of R.I.R.B. and plotted on semi-logarithmic paper. Human serum albumin, labelled with ^{131}I (R.I.S.A.) was used to determine the dose–response relationship between hepatic blood volume and external counting.

The uptake of R.I.R.B. by the liver, measured by external monitoring, was compared with the plasma removal rate of R.I.R.B., determined by measuring the concentration in multiple blood samples in the immediate post-injection period. The R.I.R.B. excretion rate was also compared with the accumulation of R.I.R.B. in the bile obtained by duodenal aspiration from 5 patients who had undergone cholecystectomy.

R.I.R.B. uptake by the liver in 20 studies on 14 normal subjects and on 8 patients whose gall-bladders had been removed occurred in a mean of 7·6 minutes, while the phase of excretion lasted 81 to 92 minutes. Between these limits there was a brief interval during which uptake balanced excretion. Major body movements, such as bending the knees or raising the arms, invalidated the records, but radiation from the dye in the gall-bladder or intestine did not affect the result significantly. The dose–response relation of R.I.S.A. in the hepatic blood was linear and constant for any one subject who remained in one position. It is possible to predict the effect of a dose of R.I.R.B. in hepatic blood in relation to total liver radioactivity provided the response to a preceding dose of R.I.S.A. is first determined; the process of calculation is expressed in a series of graphs. The curves for both removal of R.I.R.B. from the blood and its excretion from the liver were exponential and showed good correlation.

The authors conclude that while this technique gave reproducible results under optimum conditions, it is not recommended for routine laboratory use. It is nevertheless a valuable physiological method which can be applied to any substance that can be labelled with gamma-radiation-emitting isotopes. *F. Hillman*

424. **Differential Analysis of the Stages of Hepatic Excretory Function with Gamma Emitting Isotopes. II. Attempts to Alter Rate Phenomena**

E. ENGLERT JR., B. A. BURROWS, and F. J. INGELFINGER. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **56**, 193–206, Aug., 1960. 5 figs., 30 refs.

Employing the radioiodinated rose bengal (R.I.R.B.) technique described in their previous paper [see Abstract 423] the authors have investigated the rate of hepatic excretion of a number of substances. In all, 112 observations were made on 46 subjects aged from 22 to 76 years. In this series two injections of R.I.R.B. were given on each occasion. The substances studied included sodium dehydrocholate, sulphobromophthalein, sodium iodipamide (" cholografin "), non-radioactive and carrier rose bengal, heparin sodium, probenecid sodium, cortisol, chlorothiazide, chlorpromazine hydrochloride, fibrinogen-free–low-globulin plasma, and iodopyracet (" diodrast "). Most of these substances were tested in low, medium, and high dosage and the detailed results are presented in tables and graphs.

The uptake of R.I.R.B. by the liver was retarded by the previous administration of sodium dehydrocholate, sulphobromophthalein, and, to a lesser extent, by sodium iodipamide, whereas rose bengal and heparin had a slight and opposite effect. Excretion of R.I.R.B. by the liver was accelerated if sodium dehydrocholate or sodium iodipamide was given during the excretion phase, but sulphobromophthalein and rose bengal had no effect on the excretion rate, while the effect of cortisol was inconsistent. When given before the excretion of R.I.R.B. began sodium dehydrocholate, sodium iodipamide, and to a lesser extent sulphobromophthalein delayed excretion, while rose bengal and heparin slightly accelerated it.

The uptake of radioiodinated iodopyracet (R.I.D.) by the liver was faster than that of R.I.R.B. Carrier iodopyracet in large doses flushed R.I.D. from the liver and it reappeared in the blood. Non-radioactive rose bengal neither affected R.I.D. excretion nor displaced it into the blood. R.I.R.B. and R.I.D. therefore appear to be non-competitive for metabolic or physical pathways of biliary excretion. Hepatic blood flow, cellular uptake and transport, and cell-bile transfer are discussed in relation to the experimental findings.

[The multiplicity of substances used precludes any detailed summary of the results, for which the original paper should be consulted.] *F. Hillman*

425. **Rabbit Pancreas in Protein Malnutrition (Experimental Kwashiorkor) and after Cortisone Administration**
B. W. VOLK and S. S. LAZARUS. *American Journal of Pathology* [*Amer. J. Path.*] **37**, 121–135, Aug., 1960. 10 figs., 35 refs.

In the experiments described in this paper from the Jewish Chronic Disease Hospital, Brooklyn, and the Albert Einstein College of Medicine, New York, the morphological changes in the pancreas of rabbits given a low-protein, low-fat, but high-carbohydrate diet were compared with those in rabbits subjected to prolonged steroid administration. The diet, which resembled that of the poor native Jamaican in whom kwashiorkor occurs, was administered to 38 rabbits for periods up to 15 weeks. In this group a severe degree of pancreatic acinar atrophy was observed, while in 18 animals given a normal diet and cortisone for 2 to 6 weeks there was proliferation of the pancreatic ducts.

It is concluded that the proliferation of the ducts in the cortisone-treated animals is not due to the protein catabolic action of the steroid but is related to some other effect of cortisone. The acinar atrophy seen in the animals given the special diet is attributed to deficiency of protein or of essential amino-acids. *H. Harris*

426. **The Role of Incomplete Pancreatic Duct Obstruction in the Etiology of Pancreatitis**
R. E. HERMANN and J. H. DAVIS. *Surgery* [*Surgery*] **48**, 318–329, Aug., 1960. 8 figs., 18 refs.

A short review of the literature suggests that reflux of bile into the pancreatic duct is unlikely to be as common a cause of acute pancreatitis as was previously thought. An alternative hypothesis is that of intermittent or incomplete obstruction of the pancreatic outflow. In experiments carried out at Western Reserve University, Cleveland, Ohio, the major pancreatic duct in 6 mongrel dogs weighing 10 to 15 kg. was narrowed to a third of its normal diameter by ligating it over a No. 24 needle. After the animals had recovered, the pancreas was stimulated every third or fourth day by a heavy protein meal together with the subcutaneous injection of 10 units of secretin and 0·75 mg. of "urecholine". The dogs were serially killed 5, 10, 15, 20, 30, and 40 days after the operation. In another group of 10 dogs, a small polyvinyl catheter (0·044 cm. internal diameter), threaded over a stainless steel wire to give extra strength, was passed round the pancreatic duct and brought out through a larger catheter which acted as a "choker" tube. At intervals of 2 to 5 days the duct was obstructed under light anaesthesia for 2 to 4 hours, and for part of this time the pancreas was stimulated by an intravenous drip infusion of secretin, 50 units an hour, and urecholine, 1·25 mg. per hour, in 5% dextrose in saline solution.

The 6 dogs with partial obstruction were little affected. At necropsy the gland varied from being moderately "boggy" at 5 days to firm induration at 40 days. There was no gross evidence of fat necrosis or haemorrhage. Microscopically the appearance varied from classic oedematous pancreatitis at 5 days to pronounced periductal and interlobular fibrosis in all dogs killed after 14 days. The 10 dogs with intermittent obstruction were more severely ill. Microscopically, fat necrosis was present surrounding all the glands. In 4 of the 6 dogs with duct obstruction for 4 hours and stimulation for 3 hours, death occurred within a week at some time during the night, and post-mortem examination was delayed. The other 2 were therefore killed when they appeared severely ill. Macroscopically areas of haemorrhage and fat necrosis were seen only in the animals which died; but in the other 2, sections showed "striking" vascular congestion, many vessels being ruptured and bleeding into the gland.

The authors claim to be the first to demonstrate extensive vascular damage from obstruction and stimulation. They believe that they have demonstrated a possible mode of origin of all types of pancreatitis, from acute oedematous or haemorrhagic to chronic fibrotic disease. *Denys Jennings*

HAEMATOLOGY

427. **Level of Haemoglobin in Whole Blood and Red Blood-cells, and Proposed Convention for Defining Normality**
J. D. PRYCE. *Lancet* [*Lancet*] **2**, 333–336, Aug. 13, 1960. 3 figs., 44 refs.

In assessing physiological variables normal values have usually been determined from a small series of selected subjects, the criteria of normality being subjective, arbitrary, and undefined. The author of this paper from Little Bromwich Hospital, Birmingham, has attempted to avoid misleading extrapolation and describes a convention for calculating the normal mean and range from crude data. He gives statistical evidence on which to base figures for the normal values for haemoglobin (Hb), packed-cell volume, and mean corpuscular haemoglobin concentration (M.C.H.C.) in males and females.

The modal value is taken as the point of reference. A gaussian curve is superimposed on the mode and this range is defined as the arbitrary normal. First a frequency distribution is drawn up for 100 to 200 consecutive values to discover whether the curve is roughly symmetrical. If the divergence from normal is equal, the arithmetic mean and mode will coincide, but abnormal values at the tails of the curve will exaggerate the variance. In the gaussian curve 68% of the population fall within one standard deviation (S.D.) from the mean. The number equal to 34% of the total population being considered is therefore calculated, the distance of this number on each side of the mean value is interpolated, and the mean of the two deviations so obtained is then taken; this gives an approximate estimate of the S.D. which is independent of the distribution at the tails of the curve. If abnormal values in a mixed population diverge more in one direction than in the other, the mode of the distribution is moved less than is the mean or the median. If there is moderate skewing of the distribution the mode can be calculated from the formula: mean − mode = 3

(mean−median) and in a gaussian curve the distribution of results around the mode should be symmetrical. The S.D. is calculated in the same way, but only figures on the supposedly normal side of the mode are used, and this value is interpolated on the other side.

In the statistical study here described the estimation of Hb values in unselected venous blood samples from 102 adult males and 126 adult females (as determined by the cyanmethaemoglobin method, standardized by periodical estimates of the iron content of blood cells using the factor of 338 mg. of iron to 100 g. Hb) gave the following results per 100 ml.: 14·4 g.±1·34 for males and 13·3 g. ±1·34 for females, a haematocrit value of 45·1%±4·13 for males and 42·2%±4·02 for females, and a M.C.H.C. of 32·0%±1·42 for males and 32·0%±1·36 for females. It is pointed out that these values are usefully comparable with the more recently reported figures, but like the latter do not agree well with the means and ranges cited in standard textbooks, which were probably based on selected " ideal normals ". *A. Ackroyd*

428. **The Influence of Animal and Vegetable Fats on Blood Coagulability in Subjects with and without Atherosclerosis.** (Влияние животного и растительного жира на свертываемость крови у больных атеросклерозом и у не болеющих атеросклерозом лиц) V. M. Rassohin. *Терапевтический Архив* [*Ter. Arh.*] **32**, 83–86, Aug., 1960. 6 refs.

In 26 patients (21 male and 5 female) aged from 42 to 73 years suffering from atherosclerosis (Group 1) the blood coagulation time was determined before and again 5 hours after a meal consisting of 75 g. of butter and 20 g. of bread. A few days later the experiment was repeated using sunflower oil in place of butter; 20 subjects (16 male and 4 female) aged 15 to 42 years with no clinical evidence of atherosclerosis (Group 2) served as controls. Similar determinations were carried out on 10 subjects of comparable age (Group 3) who received the caloric equivalent of the fat-and-bread meal in the form of carbohydrates only. In Group 1 the ingestion of butter and sunflower oil resulted in an average shortening of the coagulation time by 23·9 and 18·3 seconds respectively, the corresponding figures for Group 2 being 22·1 and 21·5 seconds. Ingestion of carbohydrates alone, on the other hand, resulted in an increase of the coagulation time in 8 of the 10 subjects in Group 3. It is concluded that in the presence of atherosclerosis the ingestion of vegetable fat shortens the coagulation time to a lesser degree than does the ingestion of animal fat. *S. W. Waydenfeld*

429. **A Naturally Occurring Inhibitor of the First Stage of Blood Coagulation**
L. G. Israels, J. Foerster, and A. Zipursky. *British Journal of Haematology* [*Brit. J. Haemat.*] **6**, 275–280, July [received Sept.], 1960. 1 fig., 17 refs.

Adsorption of bovine plasma on asbestos shortens the Quick one-stage prothrombin time and this activation is associated with an increased Factor VII activity. At the University of Manitoba, Winnipeg, the thromboplastin generation test was used to study the effect of asbestos adsorption and the adsorbed inhibitor on the initial phases of coagulation. Asbestos adsorption of bovine and human serum resulted in a markedly accelerated thromboplastin formation as well as the generation of an increased amount of thromboplastin. The maximum generation was reached within one minute. No activation was observed by adsorption of plasma alone, but a heat-labile substance which was capable of inhibiting thromboplastin formation could be eluted with 0·14 molar sodium citrate from plasma but not from serum. The results suggest that the citrate elute of asbestos previously exposed to bovine plasma contains a substance which exerts an inhibitory action against both Factor VII and a serum factor necessary for the generation of thromboplastin, probably Christmas factor; this inhibitory substance is probably partially removed during the process of coagulation and accounts for the increased activity of Factor VII and Christmas factor in serum. *A. Ackroyd*

430. **The Concentration of Antihaemophilic Globulin (AHG) Related to Age**
A. A. Cooperberg and J. Teitelbaum. *British Journal of Haematology* [*Brit. J. Haemat.*] **6**, 281–285, July [received Sept.], 1960. 3 figs., 12 refs.

A wide variation in antihaemophilic globulin (AHG) levels has been reported in normal subjects. This study suggests that the AHG concentration tends to increase with age. At the Jewish Hospital, Montreal, 100 normal individuals (aged 17 to 78 years) were selected. It was found that while the concentration ranged from a minimum of 50% to a maximum of 195%, there was a steady rise with age from a mean concentration in males of 101% in the age group 17 to 29 years to 132% in the age group 60 to 79 years and in females from 89% to 121%. The increase was particularly notable in subjects over 40 years of age. This difference between age groups was found to be highly significant and it was noted that the mean concentration was higher in males in all age groups than in females.

The authors conclude that this increased concentration of AHG with age may be a manifestation of hypercoagulability of the blood and may predispose to thrombosis, and suggest that in the treatment of patients with haemophilia, the use of blood or plasma from the older male population may be advisable as a higher concentration of AHG may thus be administered. *A. Ackroyd*

431. **Components of Blood Necessary for Clot Retraction**
M. Corn, D. P. Jackson, and C. L. Conley. *Bulletin of the Johns Hopkins Hospital* [*Bull. Johns Hopk. Hosp.*] **107**, 90–104, Aug., 1960. 9 figs., 39 refs.

At Johns Hopkins University School of Medicine, Baltimore, the authors studied clot retraction and the constituents of the blood which are essential for this phenomenon in platelet-rich plasma containing disodium ethylenediamine tetra-acetic acid (EDTA), platelet-rich plasma containing acid-citrate-dextrose (ACD), and a purified fibrinogen–thrombin system.

Platelets, glucose, divalent cation, fibrinogen, and thrombin were found to be necessary. Retraction occurred at *p*H 6·0 and above but was absent at *p*H 5·6. Magnesium, strontium, or barium chloride was as effective as calcium in plasma containing EDTA. Sodium and chloride were present in the reacting mixtures but the specific role of these ions was not investigated. The ability of platelets to participate in retraction was rapidly lost on exposure to sonic energy, this preceding their morphological disruption. The use of serotonin instead of platelets produced no retraction. It seems likely, the authors state, that clot retraction is a function of platelets acting as cellular structures; it may be possible to use retraction function as an index of viability of stored platelets. They also state that the retraction-promoting effect of glucose and of elevation of *p*H could be demonstrated several hours after clotting had occurred and therefore the essential roles of *p*H and of glucose appear " not to be related to the manner of clot formation ".

A. Brown

MORBID ANATOMY AND CYTOLOGY

432. **Pathology of the Internal Carotid Artery.** (К патологии внутренней сонной артерии)
A. S. Ogurcova. *Журнал Невропатологии и Психиатрии* [*Ž. Nevropat. Psihiat.*] **60**, 934–939, No. 8, 1960. 4 figs., 4 refs.

The author reports a post-mortem study of 60 patients suffering from arterial hypertension who died from cerebrovascular disorders. Most of them were between 50 and 70 years of age at death, though 2 were under 50. It was established that 24 died of cerebral haemorrhage, 34 of cerebral thrombosis with softening of the brain, and 2 of myocardial infarction. At necropsy 11 were found to have complete occlusion of one or other internal carotid (the left in 6 cases and the right in 5). Histological examination revealed the presence of thromboangiitis of the artery in 2 cases, thrombo-embolic changes in 3, while sclerosis of the walls of the vessel was found in 6. (The thrombo-embolic changes arose from intracardiac thrombi.) In the cases with sclerosis the lumen was obliterated by masses of fibrous connective tissue arising from the intima, often in the absence of atheromatous plaques. The aorta was also examined, but in many cases was less seriously involved than the internal carotid artery; this, it is suggested, is probably due to the haemodynamic situation of the latter vessel and the strain to which it is subjected in maintaining the copious blood supply to the brain (averaging one litre per minute).

Such a major disturbance of the intracranial blood supply as complete occlusion of one internal carotid artery leads to secondary changes in the cerebral arteries, especially the middle cerebral, in the wall of which a laminar structure of atherosclerotic plaque forms, causing irregular narrowing of the lumen. In other vessels there is acceleration of a pre-existing atherosclerosis, while in acute occlusion of the internal carotid coagulation of the blood in a sclerosed cerebral vessel may occur if there is no compensating increase in blood supply through the circle of Willis. For these reasons the state of the circulation in the internal carotid arteries deserves more attention from clinicians than it generally receives.

L. Firman-Edwards

433. **The Pulmonary Vascular Structure of Children with Interventricular Septal Defects: a Comparison with Physiologic Studies**
H. S. Rosenberg, D. G. McNamara, R. A. Leachman, and R. M. Buzzi. *Archives of Pathology* [*Arch. Path.*] **70**, 141–148, Aug., 1960. 9 figs., 8 refs.

The medial layer of the small muscular arteries of the lung is commonly thickened in association with pulmonary hypertension secondary to ventricular septal defect in infants and children. This study would suggest that neither the presence nor the degree of medial hypertrophy can be directly correlated with pulmonary pressure or the size of the defect or the volume of the left-to-right shunt. There is a tendency for the ratio of media thickness to diameter of the vessel to diminish with age in this malformation.

In some children, the reaction of medial hypertrophy may be followed by intimal lesions consisting of cellular hyperplasia and fibrosis. Occasionally, perhaps prior to the development of intimal lesions, the medial layer assumes a configuration similar to that of a normal person of the same age despite the fact that there is no decrease in pressure. It is suggested that " vascular tone " accounts for the maintenance of pulmonary vascular resistance during this period of apparently normal anatomy of the small muscular arteries.—[Authors' summary.]

434. **Congenital Universal Insensitivity to Pain**
D. W. Baxter and J. Olszewski. *Brain* [*Brain*] **83**, 381–393, Sept., 1960. 13 figs., 28 refs.

We have presented the autopsy findings of a young woman who suffered from congenital insensitivity to pain. Her lack of pain appreciation was so great that she suffered extensive skin and bone trauma which contributed in a direct fashion to her death. Yet we were unable to demonstrate any gross abnormalities of those nervous system structures thought to be concerned with pain impulses. The possibility that the defect is actually an anatomical one, but in terms of organization rather than structure, is not excluded. The fact that the syndrome might result from perceptual or psychological variations is also discussed.—[Authors' summary.]

435. **The Histopathologic Changes of Sprue and Their Significance**
W. M. Thurlbeck, J. A. Benson Jr., and H. R. Dudley Jr. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **34**, 108–117, Aug. [received Oct.], 1960. 8 figs., 15 refs.

The variations in normal jejunal mucosa and the extent, nature, and mechanism of the mucosal changes in patients with steatorrhoea are discussed in this paper from Harvard Medical School and the Massachusetts General Hospital, Boston. The height of the villi, the depth of the crypts, and the ratio between these 2 measurements were determined in jejunal mucosa obtained from

21 patients with steatorrhoea and 11 controls. Mucosal tissue was obtained in about half the cases by peroral intubation, in 4 at necropsy, and in the remainder by surgical biopsy, the specimens being fixed in formalin within 3 minutes of excision. Measurements were made only of villi and crypts cut at right angles to the mucosal surface, 10 of each being measured in each specimen. In abnormal tissue identification of villi and crypts was difficult; nevertheless, the conclusions of two independent observers were similar.

In the controls the height of the villi ranged from 260 to 470 μ (mean 365 μ) and the depth of the crypts from 120 to 260 (mean 165) μ. The ratio was always greater than one, ranging from 1·3 to 3·7 (mean 2·2). Histologically the 21 patients with steatorrhoea could be divided into two sharply-distinguished, non-overlapping, groups. In 12 patients, all with idiopathic steatorrhoea (adult coeliac disease), the villi were short (height 75 to 200 μ, mean 135 μ), the crypts elongated (depth 180 to 450 μ, mean 285 μ), and the ratio less than one (0·19 to 0·76, mean 0·47). There was also a marked infiltration of inflammatory cells. In 9 patients, 6 of whom had other diseases causing the steatorrhoea, the villi and crypts were normal; the remaining 3 patients with normal mucosa could not be distinguished on clinical grounds from the others with idiopathic steatorrhoea. In the patients with an abnormal mucosa, there was no correlation between the severity of the clinical condition and the degree of the histological abnormality.

M. Lubran

436. **Phenylketonuria: a Review and a Report of the Pathological Findings in Four Cases**
L. Crome and C. M. B. Pare. *Journal of Mental Science* [*J. ment. Sci.*] **106**, 862–883, July [received Oct.], 1960. 15 figs., bibliography.

The authors of this paper from the Fountain and the Bethlem Royal and Maudsley Hospitals, London, present a very complete review of the biochemical background and the clinical and pathological features of phenylketonuric oligophrenia. Discussing the extensive literature on the pathogenesis of the condition the authors state that the primary abnormality is an inability of the liver to hydroxylate phenylalanine to tyrosine, the fault being probably due to the absence or inactivity of an unstable fraction in the enzyme system responsible for this step. The mental defect, on the other hand, is likely to be due to an inhibition by other metabolites of phenylalanine of various enzyme systems in the brain not yet specified. The foetus is protected *in utero* by the maternal liver, so that the metabolic defect only becomes manifest a few weeks after birth. Dietary control should be instituted as soon as the metabolic defect is detected.

The incidence of phenylketonuria is about 4 per 100,000 live births. Mental deterioration shows itself during the first few weeks or months of life, but the rate of progress and the ultimate severity of the defect varies considerably. A few affected infants (1%) have an intelligence quotient (I.Q.) of over 70, but in the majority it is below 40. Epilepsy, both major and minor, is common and patients with severe mental defect often show signs of extrapyramidal disease. The metabolic disorder is diagnosed by simply adding 5% solution of ferric chloride to the urine; if phenylpyruvic acid is present an olive-green colour quickly develops, which fades in 15 to 30 minutes. Anatomical lesions in the brain are few.

The authors analyse the 20 cases reported in the literature and describe in detail 4 of their own. The brains of these patients are small and about half of them showed patchy areas of pallor in myelin-stained preparations. It is not clear whether this finding is due to a defect of myelin formation or the result of a demyelinating process; it is accompanied by gliosis.

The chief therapeutic measure is a diet low in phenylalanine. This should restore the blood phenylalanine level to normal and result in substantial improvement in the infant's general health and in hair pigmentation, with clearance of any skin changes. Epilepsy is strikingly reduced, but the effect on the I.Q. is problematical. If the diet is started before the child is 2 years old the mental deterioration will be slowed, if not halted; if it is not started until after 4 years of age irreversible changes will probably have occurred. *J. B. Cavanagh*

437. **The Liver in the Aging Process: Histology**
R. D. Carr, M. J. Smith, and P. G. Keil. *Archives of Pathology* [*Arch. Path.*] **70**, 1–4, July, 1960. 4 figs., 8 refs.

The histological appearances of the liver at necropsy in patients aged 60 years and over were compared with those in patients aged 20 to 30 years. All the patients (55) had died from traumatic causes in a matter of minutes to a few hours and no previous medical history was known. Although in several cases there was definite evidence of hepatic disease, it became apparent that the changes associated with the ageing process were not related to the pathological changes of organic disease. The authors' findings confirm those of Andrew *et al.* (*Amer. J. Anat.*, 1943, **72**, 199), who found the following senile hepatic changes present in mice and human beings: (1) giant parenchymal cells, (2) giant hyperchromic, irregular, aberrant nuclei, (3) multiple nucleoli (5 to 15) within the giant nuclei, (4) binucleate cells, and (5) a clear perinuclear zone.

In the present series of patients three distinct groups were recognized: (1) 35 patients (19 old and 16 young) whose livers showed the characteristics of their age-group (senile changes in the elderly and absence of these in the young); (2) 3 patients (one old and 2 young) in whom the histological picture was so misleading that the age-group was incorrectly deduced; and (3) 17 patients (13 old and 4 young), whose livers showed characteristics of both the senile and the young and the age-group could not be determined with any high degree of accuracy.

[This investigation is interesting, but the number of exceptions to the "classic" picture does indicate that aetiological factors other than age should also be considered, since exposure to other agents would, presumably, be more likely in the old than in the young.]

W. H. Horner Andrews

Microbiology and Parasitology

438. **Studies on an Attenuated Measles-virus Vaccine. I. Development and Preparation of the Vaccine: Technics for Assay of Effects of Vaccination**

J. F. ENDERS, S. L. KATZ, M. V. MILOVANOVIĆ, and A. HOLLOWAY. *New England Journal of Medicine* [*New Engl. J. Med.*] **263**, 153–159, July 28, 1960. 30 refs.

It has been shown that measles virus adapted to growth in chick-embryo cell cultures loses some of its pathogenic powers while retaining its antigenic properties. The avianized attenuated measles virus is distinguished from the original virus by its capacity to multiply and to induce cytopathic effects in chick-cell systems, by its incapacity to produce overt disease or consistently recognizable viraemia in susceptible monkeys, and by its incapacity to multiply freely in the central nervous system of monkeys or to establish itself in the upper respiratory tract following intracerebral inoculation. In spite of these changes in its properties inoculation into monkeys by parenteral routes produces complement-fixing and virus-neutralizing antibodies in high concentrations between the 15th and 23rd days and in lower concentration for long periods afterwards.

On the basis of these studies limited trials of two vaccines were carried out in susceptible patients at the Children's Hospital Medical Center, Boston. (Details of the preparation of the vaccines are given.) Vaccine A was prepared from a stored pool of attenuated virus which was inoculated into tissue culture bottles and harvested after 11 days. Sufficient human albumin, which was 5% in most batches but 2·5% in a small batch, was added as a stabilizer. Vaccine B was prepared from the same original strain of measles virus except that the virus was passed through a further 6 serial chick-embryo cultures before being cultured for production of the vaccine and only 1·1% human serum albumin was added as a stabilizer. Exhaustive tests of the sterility of the vaccine and its freedom from local or general toxinic action were carried out. Before the vaccines were given they were tested in adults whose serum contained measles antibodies. The vaccine thus prepared was stored at a temperature of −55° to −60° C. and remained unchanged for at least 3 years. During the clinical trial attempts were made to culture the virus from the blood stream and from secretions from the throat and larynx. Neutralization and complement-fixation tests were also carried out on specimens of serum.

In general it was found that there was a direct correlation between resistance and the presence of antibodies in the serum, even though the antibodies were very weak. In some patients neutralizing antibody was detected in the absence of a positive reaction to the complement-fixation test; this was sufficient for such subjects to resist infection either with the chick-embryo attenuated strain or the measles virus itself. *R. F. Jennison*

439. **Studies on an Attenuated Measles-virus Vaccine. VIII. General Summary and Evaluation of the Results of Vaccination**

S. L. KATZ, C. H. KEMPE, F. L. BLACK, M. L. LEPOW, S. KRUGMAN, R. J. HAGGERTY, and J. F. ENDERS. *New England Journal of Medicine* [*New Engl. J. Med.*] **263**, 180–184, July 28, 1960. 12 refs.

An evaluation of the results of the first clinical trials of an attenuated measles-virus vaccine [see Abstract 438] is presented. The vaccine was given to a total of 303 children—orally, intranasally, or via the conjunctiva in 31 and by subcutaneous or intradermal injection in 272. Most of the observations are therefore based on the children who received the vaccine parenterally.

There was no significant difference, clinically or serologically, between the two vaccines (A and B) so they were considered together. Of the 272 children inoculated parenterally none experienced an immediate or local reaction. No clinical or serological response was detected in 101 children who were judged to be immune beforehand on the basis of pre-existing antibodies. Clinical reaction to vaccination in 171 susceptible children consisted principally in fever (83%) and a modified rash (48%). Koplik's spots were looked for in 111 of this group but were detected in only 16%. No catarrhal signs and no bacterial complication such as bronchopneumonia or otitis media occurred. There was no evidence of central nervous system involvement in any of the patients. In 31 vaccinated children from whom blood and throat secretions were taken at intervals, repeated attempts to isolate the virus were unsuccessful. Transmission of the disease was not observed in any of 143 susceptible contacts. Serological response to vaccination was demonstrated in 96·5% of the 171 children who had no antibodies before vaccination; in all these cases the serum was tested for complement-fixing antibodies and the failure of a few to respond was probably accounted for by the existence of neutralizing antibody. The actual antibody titres detected were quantitatively comparable to those following natural measles infection. The authors state that the ultimate persistence of the antibody is not known, but in some patients levels were maintained for 18 months after immunization.

Of the routes of vaccination, other than parenteral, only the intranasal route resulted in a significant number of serological responses. The vaccine produced a highly effective degree of protection against measles, as shown by the fact that of 44 vaccinated children in direct contact with cases of the disease, none developed measles; in a non-vaccinated group the expected rate of infection would have been at least 70%. The interval between vaccination and the development of immunity was not precisely determined, but in a few children exposed to infection within 10 days of vaccination measles did not develop.

The desirability and acceptability of general vaccination against measles are discussed. The majority of deaths are due either to secondary bacteriological infections or to involvement of the central nervous system. The success obtained in the present series of cases suggests that more extensive clinical trials of the attenuated measles-virus vaccine should be carried out. Further work is in progress directed towards producing a vaccine which may induce as good a serological response with fewer febrile reactions; in addition, the problem of storage of the vaccine over long periods has still to be solved. *R. F. Jennison*

440. **Respiratory Flora of Hospital-related Populations** R. S. BENHAM, I. HAVENS, and J. J. LANDY. *Journal of Infectious Diseases* [*J. infect. Dis.*] **107**, 1–10, July–Aug., 1960. 6 figs., 9 refs.

The results of a long-term study of organisms isolated from the upper respiratory tract of "hospital-related" populations are reported in this paper from the University of Chicago Clinics. The 2,000 volunteers included surgeons, general practitioners, a group of subjects indirectly associated with the hospital, and a group unrelated to the hospital. In 1952 culture of nasopharyngeal swabs revealed that 43% of surgeons in the hospital carried antibiotic-resistant *Staphylococcus aureus* in the upper respiratory tract; in 1958 this figure was 10%. Over the same period the percentage of carriers of organisms of the enteric group rose from 5 to 24. A comparable alteration in flora was seen over the same period in infected clean wounds. A significant carrier rate for *Staph. aureus* was observed only when there was direct, heavy, and continuous contact with patients. This, however, was not true of the organisms of the enteric group; indeed, a rise in the carrier rate of enteric organisms occurred in all populations irrespective of their hospital associations. The phage types of *Staph. aureus* appearing in various situations were also studied, and the authors comment on the occurrence of "epidemic" strains such as the Type 80/81 in non-surgical departments.

There appeared to be regional differences in carrier rates of various organisms in the respiratory tract, but the authors state that these were "neither regular nor constant and interpretation of them requires more study". *A. E. Wright*

441. **A New Screen Test and Selective Medium for the Rapid Detection of Epidemic Strains of *Staph. aureus*** B. MOORE. *Lancet* [*Lancet*] **2**, 453–458, Aug. 27, 1960. 3 figs., 12 refs.

Phage-typing of staphylococci shows that relatively few strains are responsible for epidemics of hospital cross-infection. In this paper from the Public Health Laboratory, Exeter, a rapid method of recognizing these potentially dangerous strains is described. The method developed from an observation that catgut from infected wounds seemed soft. Experiments with batches of catgut showed that one batch appeared to inhibit the growth of some staphylococcal strains. Eventually this inhibition was found to be due to mercuric ions in the form of mercuric iodide used in one of the stages of preparation of the catgut. Further investigation revealed that Type-80 strains and some Group-III staphylococci grow in higher concentrations of mercury than other strains of *Staphylococcus aureus*.

This method of differentiation was shown by agar-plate inhibition tests on a series of 50 unselected staphylococcal strains employing filter paper strips impregnated with 1:1,000 phenylmercuric nitrate. Similar inhibition occurred using a peptone–agar base containing 1:27,800 mercuric chloride. The staphylococci examined in this way fell clearly into two groups, suggesting that this resistance to mercuric ions was a real difference. It was not obtained when silver, copper, or cobalt salts were used.

The method was employed on a series of 505 staphylococci and revealed that of 113 strains of Phage-type 80 no fewer than 107 showed resistance to mercuric ions and of 31 strains of Phage-type 52/52A/80 no fewer than 30 were resistant. All Phage-group I strains without an 80 in their phage pattern were mercury sensitive as were the majority of other "non-epidemic" strains of staphylococci.

The authors claim that the use of media incorporating mercuric-ions with added milk provides a rapid method of detecting potentially epidemic strains of staphylococci, although they point out that it does not follow that mercury-sensitive staphylococci are unimportant. *A. E. Wright*

442. **An Outbreak of Brucellosis in Man Due to the Migration of *Brucella melitensis* to Cattle** (Эпидемическая вспышка бруцеллеза, обусловленная миграцией Br. melitensis на крупный рогатый скот) A. A. MOLDAVSKAJA, A. A. LIFŠIZ-VASIL'ČENKO, M. K. JANČENKO, I. I. POLJAKOV, and V. S. URALEVA. *Журнал Микробиологии, Эпидемиологии и Иммунобиологии* [*Ž. Mikrobiol.* (*Mosk.*)] **31**, 113–117, Sept., 1960. 1 fig., 12 refs.

The greater clinical severity of brucellosis due to *Brucella melitensis* infection in man as compared with that due to *Br. abortus* has drawn attention to the epidemiological risk involved when herds of cattle become infected with *Br. melitensis*. Only a few outbreaks of the disease due to infected cow's milk have been described. In this paper the authors describe one of these rare outbreaks, which occurred in 1957 in the district of Lgansk. It could be traced to milk from cows grazing together with infected sheep near a certain village. In all, 68 persons were affected, 14 cases occurring in the village itself and 54 in a neighbouring industrial town to which raw milk had been delivered from the village. *Br. melitensis* was isolated from blood cultures of 2 patients and from the milk of 2 cows. *K. Zinnemann*

443. **The Viral Etiology of Neoplasms—a Review** E. A. MCCULLOCH. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **83**, 1049–1063, Nov. 12, 1960. 12 figs., bibliography.

Pharmacology and Therapeutics

444. **The Analgesic Potency of Piminodine (Alvodine)**
T. J. DeKornfeld and L. Lasagna. *Journal of Chronic Diseases* [*J. chron. Dis.*] **12**, 252–257, Aug., 1960. 3 refs.

Piminodine is a derivative of pethidine but differs from it in that 3(phenyl-amino) propyl replaces a methyl group on the nitrogen atom of the piperidine ring. Its analgesic potency has been studied at the Baltimore City Hospitals in 96 patients suffering from postoperative pain and compared with that of 10 mg. of morphine. When patients asked for an analgesic they were given, subcutaneously, 10 mg. of morphine alternating with piminodine, the dose of the latter being 5 mg. in one group of patients, 10 mg. in a second, and 20 mg. in a third. The patients were unaware of the nature of the medication as were the doctors who inquired about pain and other symptoms over the 4 hours following each injection.

By simple methods of scoring, based on four degrees of pain, it was found that 5 mg. of piminodine was less effective than 10 mg. of morphine, but that piminodine in a dosage of 10 or 20 mg. was more effective. The degree of sedation with piminodine was no greater than with morphine and there were only two episodes of vomiting, both of these in patients receiving 20 mg. of the drug.

It is stated that further studies on side-effects, such as respiratory depression, are needed and are already planned.

T. B. Begg

445. **A Clinical Study of Triparanol (MER–29)**
P. Lisan, W. Oaks, and J. H. Moyer. *American Journal of Cardiology* [*Amer. J. Cardiol.*] **6**, 246–251, Aug., 1960. 4 figs., 5 refs.

At Hahnemann Medical College and Hospital, Philadelphia, triparanol was given in a dosage of 100 to 1,000 mg. daily for 12 to 15 months to 45 patients with arteriosclerotic heart disease and a serum cholesterol level exceeding 250 mg. per 100 ml. It is stated that the drug inhibits the synthesis of cholesterol, probably at the level of conversion of 24-dehydrocholesterol to cholesterol. No significant changes in the serum cholesterol level were observed with a dosage of 100 mg. daily, but with 250 mg. daily there was a fairly gradual and with 500 and 1,000 mg. daily a more precipitous fall in the serum cholesterol level. Combined results with all dosages showed a significant fall in 39 (87%) of the patients, which amounted to more than 75 mg. per 100 ml. in 23 (51%).

The effects of the drug remained constant during continued administration, but when the drug was withdrawn the serum cholesterol level climbed slowly toward control values, to fall again when administration was resumed. The higher the initial cholesterol level, the greater the reduction induced by the triparanol. The haemoglobin level, haematocrit value, leucocyte count, and blood urea-nitrogen level were determined, but did not reveal any evidence of toxic side-effects. The authors state that a 5-to-10-year study is needed to determine the influence of this drug on the prognosis in coronary artery disease. In view of the possible effect of 24-dehydrocholesterol on the colorimetric determination of the serum cholesterol level re-evaluation of the methods used for the latter might become necessary. [Those interested in this drug may find it worth while to consult the paper by Avigan *et al.*, *Progr. cardiov. Dis.*, 1960, **2**, 485.]

A. Schott

446. **The Acute and Long-term Effects of Guanethidine on Renal Haemodynamics and Water and Electrolyte Exchange in Healthy Subjects.** (Über die akute und protrahierte Wirkung von Guanethidin auf die Nierenhämodynamik, den Wasser- und Elektrolythaushalt bei gesunden Personen)
D. P. Mertz. *Deutsche medizinische Wochenschrift* [*Dtsch. med. Wschr.*] **85**, 1278–1281, July 9, 1960. 16 refs.

The author, working at the University of Freiburg, has investigated the short- and long-term effects of guanethidine on renal function in 10 healthy adults who received 20 mg. of the drug intravenously. This was followed by the serial determination of the clearance of inulin and PAH, the extracellular fluid volume, and the rate of excretion of sodium, potassium, and calcium, as well as of the total volume of urine. The serum electrolyte levels and blood pressure were also measured before and after the administration of the drug in all the patients.

In 8 subjects the effects of guanethidine were most marked after 30 minutes and in the remaining 2 between 30 and 60 minutes later, these consisting in reduced clearance of both inulin and PAH initially, followed by a rise. No change in the extracellular fluid volume was observed, but there was a marked fall in the urinary excretion of sodium, potassium, and calcium, which however did not affect the serum levels of these ions. These results are interpreted as indicating an increased resistance in the renal vascular bed, the main site being the afferent arterioles.

In 5 healthy subjects who received 10 mg. of guanethidine orally daily for 5 to 7 days no change in blood pressure was noted, but there was a significant increase in PAH clearance. There was no change in the urinary excretion of sodium, potassium, or calcium.

H. F. Reichenfeld

447. **Clinical Evaluation of Methindethyrium Chloride in Hypertension**
H. G. Smith and M. S. Klapper. *Antibiotic Medicine and Clinical Therapy* [*Antibiot. Med.*] **7**, 605–612, Oct., 1960. 3 figs., 4 refs.

Chemotherapy

448. **Comparative Clinical Effectiveness and Toxicity of Vancomycin, Ristocetin, and Kanamycin**
B. A. Waisbren, L. Kleinerman, J. Skemp, and G. Bratcher. *Archives of Internal Medicine* [*Arch. intern. Med.*] **106**, 179–193, Aug., 1960. 1 fig., 17 refs.

Ristocetin, vancomycin, and kanamycin were alternately administered to 131 patients with severe staphylococcic infections or bacterial endocarditis, the groups of patients receiving each drug being comparable. Each drug was effective in slightly over one-third of the patients studied. No one antibiotic showed marked clinical superiority over the others.

Significant ototoxicity and nephrotoxicity were found with ristocetin, kanamycin, and vancomycin. Ristocetin also caused a high incidence of skin reactions and depression of the granulocytic series of white blood cells in some patients. It is concluded that all three are effective antistaphylococcal agents of approximately comparable activity. They all exhibit toxicity greater than that found with the tetracyclines, penicillin, chloramphenicol, and erythromycin. Therefore, ristocetin, vancomycin and kanamycin should be used only in cases that have not or are not likely to respond to safer antibiotics and in which the condition of the patient justifies the risk of serious toxic reactions.—[From the authors' summary.]

449. **Observations on Penicillin " B "**
R. W. Fairbrother and G. Taylor. *Lancet* [*Lancet*] **2**, 400–402, Aug. 20, 1960. 8 refs.

A comparative study of the absorption of phenethicillin (penicillin " B ") and of phenoxymethylpenicillin after oral administration in 18 adult volunteers is reported. Several days elapsed between administration of the two penicillins, both of which were given in 250-mg. tablets under semi-fasting conditions. Specimens of serum, taken 40 to 80 minutes after each antibiotic had been given, were tested in serial dilutions against a sensitive *Staphylococcus aureus* strain T 91. The amount of both penicillins absorbed showed considerable individual variation. The serum level of phenethicillin ranged from 1·08 to 6·72 μg. per ml., while that of phenoxymethylpenicillin ranged from 0·48 to 4·32 μg. per ml. The average level and the individual absorption of the former were higher than those of the latter drug. In 14 of the volunteers serum levels of phenethicillin were higher than those of phenoxymethylpenicillin.

Tests *in vitro* of the relative activity of benzylpenicillin, phenethicillin, and phenoxymethylpenicillin against 35 sensitive strains of *Staph. aureus* gave essentially identical results, minimum inhibitory concentration (M.I.C.) ranging from 0·03 to 0·06 μg. per ml. A total of 70 resistant strains were also tested; with 55 (79%) there was no significant difference between benzylpenicillin and phenethicillin, but with 15 (21%) benzylpenicillin gave an M.I.C. 4 or 8 times greater than that of phenethicillin. The activity of benzylpenicillin and phenethicillin against resistant strains of *Staph. aureus in vitro* apparently depended mainly on the technique used, and especially on the final dilution of the bacterial inoculum and the duration of incubation of the tests. Phenethicillin differed little from benzylpenicillin when a heavy inoculum was used, but there was a marked difference with some strains when the inoculum was diluted, phenethicillin tending to be more active under such conditions.

The authors consider that phenethicillin cannot be recommended for the treatment of resistant staphylococcal infections, because of the possible high penicillinase content of the lesions. In such cases erythromycin, novobiocin, or vancomycin should be given.

Joyce Wright

450. **The Effect of Actinomycin D on Childhood Neoplasms**
R. K. Shaw, E. W. Moore, P. S. Mueller, E. Frei III, and D. M. Watkin. *A.M.A. Journal of Diseases of Children* [*A.M.A. J. Dis. Child.*] **99**, 628–635, May, 1960. 6 figs., 17 refs.

The antitumour action, toxicity, and metabolic effects of actinomycin D, which has been given in the treatment of neoplastic disease in children, were studied at the National Cancer Institute, Bethesda, Maryland. Crystalline actinomycin D was dissolved in 0·9% solution of sodium chloride in a concentration of 20 μg. per ml. The drug deteriorated at room temperature and in sunlight and was therefore stored at 0° C. It was administered intravenously as an isotonic saline solution over a period of 1 or 2 hours or directly into the intravenous tubing over a few minutes. A total of 21 courses of treatment with this drug were given to 12 children with metastases or local recurrence of neoplasms; one patient with Wilms's tumour received irradiation in addition. In all the patients haematological values and renal function were normal. After treatment the haemoglobin level and the leucocyte and platelet counts were determined at least twice a week. Palpable masses were measured at weekly intervals and metastases studied radiologically every two weeks. Antitumour responses were observed in 3 out of 5 patients with Wilms's tumour, in 3 out of 5 with embryonal rhabdomyosarcoma, and in one out of 2 with neuroblastoma. The regressions were often dramatic but of short duration and the patients became increasingly refractory to the drug with repeated courses of treatment. Nausea and vomiting, leucopenia, thrombocytopenia, and, as a late development, alopecia, were the major toxic effects. Radiation dermatitis was noted in the one child receiving irradiation, but in this case all toxic reactions cleared up within 3 weeks. The optimal dose in children was 75 to 100 μg per kg. body weight. The marked antitumour action of actinomycin D suggests that it merits further investigation, but the transient nature of this effect detracts from its value.

Anne Tothill

Infectious Diseases

451. **Routine Immunization with Orally Administered Attenuated Poliovirus. A Study of 850 Children in an American City**

J. S. PAGANO, S. A. PLOTKIN, C. C. JANOWSKY, S. M. RICHARDSON, and H. KOPROWSKI. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **173**, 1883–1889, Aug. 27, 1960. 18 refs.

Recent epidemics of poliomyelitis in the United States have occurred chiefly in the crowded, poorer sections of cities and affected particularly children under 5 years of age. The need for new methods of immunization, especially in infants under 6 months, prompted the Department of Public Health, Philadelphia, in the spring of 1959 to examine the feasibility of early immunization of normal children aged 6 weeks to 6 years (mostly negroes), living in two low-income districts of the city. The children, none of whom had received Salk vaccine, were given monovalent vaccines by mouth at monthly intervals in the following order CHAT (Type 1), W-Fox (Type 3), and then P-712 (Type 2). Altogether 850 Type-1, 805 Type-3, and 335 Type-2 vaccinations were given in milk or cocoa. All three types of vaccine were given to 335 children out of a total of 850; over one-half of the children in the series were under 6 months of age.

Serological sampling revealed that 44% of all the children and 66% of those 4 months to 3 years old were without any poliomyelitis antibodies before vaccination; in virtually all children between 6 and 12 months of age the antibody titre had fallen to non-detectable levels. Although there was one death, that of a 3-month-old child, due to an unexplained cause, no illnesses that could be attributed to the vaccination were encountered. A significant antibody response was noted in 91 to 100% of those children who had not yet lost maternal antibodies, while in 84 to 100% of those more than 6 months old who had no antibodies before vaccination a fourfold rise in titre occurred. The proportion of children with antibodies to all three types of virus increased from 19 to 85% after vaccination. The authors state that none of the 22 cases of poliomyelitis in Philadelphia in 1959 occurred in vaccinated children or in their households.

A. Ackroyd

452. **Studies on Smallpox and Complications of Smallpox Vaccination**

C. H. KEMPE. *Pediatrics* [*Pediatrics*] **26**, 176–189, Aug., 1960. 15 figs., 7 refs.

It is well known that it is sometimes difficult to vaccinate a very young child against smallpox, owing probably to its passive immunity. This observation led to the development of hyperimmune vaccinal gamma-globulin, and in this report from the University of Colorado School of Medicine, Denver, the author describes his experience with such a gamma-globulin in 300 patients suffering from serious complications of smallpox vaccination. It was used prophylactically in 44 children suffering from eczema, but for therapeutic reasons in 62 with generalized vaccinia, 132 with eczema vaccinatum, 23 with vaccina necrosum, 12 with vaccinia encephalitis, and in 27 cases of auto-inoculation, the doses injected varying from 0·6 to 1·2 ml. per kg. body weight. The hyperimmune gamma-globulin had no effect in 3 of the 12 children with vaccinia encephalitis and they died. Of the 28 cases of auto-inoculation 27 did well on this treatment, but 9 of the patients with eczema vaccinatum and 2 with vaccinia necrosum died. Haemagglutinating antibodies appear at the height of the reaction in an uncomplicated vaccination, but on the other hand defective formation of haemagglutinating and neutralizing antibodies favours the development of a viraemia, which leads to serious complications. The author concludes that the advantage of the treatment with hyperimmune vaccinal gamma-globulin is dependent upon the generation of sufficient antibodies to terminate the viraemia and to prevent the development of further lesions.

Franz Heimann

453. **Staphylococcal Septicaemia and Pyaemia**

D. R. HAY. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **29**, 313–331, July [received Sept.], 1960. 17 refs.

During 1957 and 1958 a total of 71 patients with bacteriaemia due to staphylococci were treated at Christchurch Hospital, New Zealand. The bacteriaemia was a complication of wound infection in 20 patients (including 4 with diabetes and one with lymphatic leukaemia) and secondary to osteomyelitis in 19, to boils or carbuncles of the face in 4, and to infection of the umbilicus in 4 (all infants); endocarditis was the cause in 6 patients. Of 20 patients in whom the infection was due to penicillin-sensitive strains 7 died in spite of treatment. There were 29 deaths among patients with infection due to organisms resistant to penicillin. *R. Hare*

454. **The Significance of *Candida albicans* in Human Sputum**

G. L. BAUM. *New England Journal of Medicine* [*New Engl. J. Med.*] **263**, 70–73, July 14, 1960. 3 figs., 37 refs.

Sputum specimens from 55 patients, 34 hospital employees and 30 healthy medical students, were studied for the presence of fungi. Fifty-five per cent of the patients, 36 per cent of the hospital employees, and 20 per cent of the medical students yielded sputum specimens positive for candida species. Approximately half these species were identified as *Candida albicans*. One medical student produced sputum that yielded a nonpathogenic cryptococcus. It is believed that the source of the candida found in the sputum specimens was the mouth and that little significance can be attached to the finding of candida in the sputum in the diagnosis of candiasis of the lung.—[Author's summary.]

Tuberculosis

455. **Study of Micro-organisms Isolated from 289 Cases of Primary Tuberculosis in Childhood.** (Étude des germes isolés de 289 tuberculoses initiales de l'enfant)
M. KAPLAN and B. DOBROWOLSKI. *Archives françaises de pédiatrie* [*Arch. franç. Pédiat.*] **17**, 605–626, 1960.

The authors describe the cultural and biological characteristics and resistance to antibiotics of the tubercle bacilli isolated from 289 children aged 1 to 15 years treated for tuberculous disease at the Hôpital Bretonneau, Paris, between 1955 and 1959. Half (143) of the patients were under 4 years of age and culture or guinea-pig inoculation proved positive for tubercle bacilli more frequently in this age group and in those aged 10 to 15 than in the children aged from 4 to 10 years. About 66% of the patients had pulmonary tuberculosis and the isolation rate from them was 50%. Another 20% were cases of tuberculin conversion without radiological signs of pulmonary disease and the isolation rate from this group was 60%.

Of the 135 strains isolated, 127 were of human type, 7 were bovine, and 1 (" paratuberculous ") was chromogenic and avirulent for guinea-pigs. Resistance to streptomycin in a concentration of 1 μg. per ml. was noted in 3% of strains isolated initially and this proportion was no higher among strains isolated at the end of the study. About 4% of the strains isolated before 1957 were resistant to isoniazid in a concentration of 1 μg. per ml., compared with 10% after that date. Only one strain, which was of attenuated virulence, showed no catalase activity and it retained the property of cord formation in Youman's medium. Staining with neutral red or with Nile blue was found to be of no value in characterizing the strains. *Janice Taverne*

456. **A Tuberculin Survey in a Large Urban Area**
A. H. GRIFFITH, M. J. BELLAMY, and J. K. MCFARLANE. *Tubercle* [*Tubercle* (*Lond.*)] **41**, 233–238, Aug., 1960.

With the object of detecting tuberculin converters among children, and through them patients with active disease, tuberculin-testing of all children over the age of one year was started in Cardiff in 1958, and in this paper the results of the first year are presented. Altogether 34,917 school-children, representing 83% of the school population, and 3,460 children under school age (20% of the possible total) were tested by the Heaf percutaneous technique, positive reactions being graded as follows: Grade 1, four or more indurated papules; Grade 2, an unbroken ring; Grade 3, a plateau of induration; and Grade 4, more severe than Grade 3. Only 11% of all tuberculin-positive B.C.G.-vaccinated children gave a Grade-3 or Grade-4 reaction, compared with 53% of unvaccinated positive reactors. A total of 1,509 unvaccinated children over the age of 5 gave Grade-3 or Grade-4 reactions to the Heaf test. Of these, 113 (7%) were already under supervision at the local chest clinic and 182 (12%) did not attend the clinic through indifference or lack of cooperation on the part of the parents. Altogether 1,214 children attended the clinic, and of these 7 —that is, nearly 6 per 1,000—were later notified as having progressive pulmonary tuberculosis; a further 17 were considered to have inactive disease and were being kept under observation. Of the 35 unvaccinated children under 5 years who were tuberculin-positive 3 had progressive tuberculosis and one had an inactive lesion. Of 1,011 adult contacts of tuberculin-positive infants and hypersensitive school children 13 were found to be suffering from active tuberculosis. *A. E. Wright*

457. **Serial Tuberculin Testing of Young Children in a London Borough**
J. A. KEEPING and R. CRUICKSHANK. *Tubercle* [*Tubercle* (*Lond.*)] **41**, 239–246, Aug., 1960. 1 fig., 17 refs.

An investigation was carried out into the tuberculin state of 4,833 children aged 0 to 5 years in Paddington, London. The proportion of positive reactors to the tuberculin-jelly test increased from 0·4% at 2 years to 1·9% at 5 years.

Of infected children 54% showed clinical or radiographic evidence of disease but there were no deaths from tuberculosis during the period of the investigation. A source of infection was found for 60% of the positive reactors and the 2 children with miliary and meningeal tuberculosis were in close contact with active adult tuberculosis. There was no demonstrable relationship between evidence of disease other than the positive tuberculin test and social class. The jelly test emerged as a reliable index of the presence of tuberculin sensitivity in this age group, giving no false negative and only 0·5% false positive reactions when compared with the 10 t.u. Mantoux test. However, the Heaf multiple-puncture test has advantages over the jelly test in tuberculin surveys in young children.—[From the authors' summary.]

458. **Observations on Vaccinating Schoolchildren with Danish Fresh B.C.G.**
K. N. IRVINE and A. BARR. *British Medical Journal* [*Brit. med. J.*] **2**, 1119–1121, Oct. 15, 1960. 4 refs.

In the Oxford Region 8,990 13-year-old schoolchildren were vaccinated with Danish fresh B.C.G. during the school year 1956–7; in 5,390 children the pre- and post-vaccination test was a Mantoux 10 T.U. P.P.D. and in 3,600 the Heaf multiple-puncture test was used. An analysis of the conversion rate and of the size of the local reaction to vaccination was made according to the interval in weeks (6 to 19) after vaccination.

In the Mantoux series the conversion rate between 7 and 18 weeks after vaccination remained within the range 93·7 to 100% and showed no tendency to decline or increase. In the Heaf series the conversion rate rose from 94·1% at six weeks to between 99 and 100% from 11 to 19 weeks; this increase in the conversion rate with

the Heaf test was probably not due to the interval from vaccination. The average diameter of the local reaction to vaccination did not vary by more than 3 mm. in either series over the period of observation. In the Heaf series the conversion rate of those who had no local reaction was 35%; in those who had a local reaction, however small, the conversion rate was 99·6%. In the Mantoux series it was found that the diameter of the Mantoux reaction had a direct relationship to the diameter of the vaccination papule.

The presence of any local reaction to intracutaneous vaccination with Danish fresh vaccine may be regarded as an indication of successful vaccination. Only persons with no local reaction to vaccination require a conversion test.—[Authors' summary.]

459. **A New Face of Tuberculosis**
F. T. ROQUE. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **240**, 17–20, July, 1960. 6 figs.

The author describes from the U.S. Army Hospital, San Francisco, the cases of 4 patients, of whom 3 showed all the signs and symptoms of pulmonary tuberculosis and one those of tuberculous pleurisy. Treatment with isoniazid (10 to 16 mg. per kg. body weight per day) together with PAS and pyridoxine in standard dosage resulted in such a rapid clinical recovery, with equally rapid clearing of the radiological picture, that one month later the original diagnosis was questioned on transfer of the patients elsewhere. However, bacteriological confirmation of the diagnosis of tuberculosis by examination of the sputum cultures and pleural fluid was available in 3 of the 4 cases. It is pointed out that this unusually rapid clearing of the radiological signs of pulmonary tuberculosis, which however is likely to occur only in recent and previously untreated cases, constitutes a danger in that it may confuse the diagnosis if it is not recognized that in some cases the signs even of tuberculosis may clear as rapidly as those of bacterial pneumonia in response to treatment.

J. Robertson Sinton

460. **Experience with Nicoteben in the Treatment of 578 Cases of Pulmonary Tuberculosis.** (Klinische Erfahrungen mit der Nicotebenbehandlung bei 578 Lungentuberkulosekranken)
B. HERTWIG and C. VIRCHOW. *Tuberkulosearzt* [*Tuberk.-Arzt*] **14**, 530–542, Aug., 1960. 6 figs., 9 refs.

From Falkenstein Sanatorium, Taunus, Hessen, the authors report the results in 578 cases of pulmonary tuberculosis which were treated with "nicoteben", a tuberculostatic drug containing 80% isoniazid and 20% *iso*nicotinaldehyde-thiosemicarbazone. This preparation seemed to be superior to isoniazid alone and the best results were obtained when treatment was maintained over at least a year. The daily dosage varied between 4 and 5 mg. per kg. body weight initially, but was later increased to 6 or 8 mg. per kg. In the over-all assessment 262 patients (45%) showed a very good result, 141 (42%) improved, the drug was ineffective in 51 (8·7%), and 24 (4·2%) deteriorated. Younger patients up to the age of 30 years responded better than older patients, and fresh lesions better than chronic ones. The combination of nicoteben with streptomycin increased the number of good results considerably. Side-effects were noted in 190 cases (33%), the most frequent being gastro-intestinal (86 cases) and nervous disturbances (65 cases), but the drug had to be withdrawn in only 36 cases.

Franz Heimann

461. **Supplementary Prednisolone in Treatment of Tuberculosis of Various Types and during Pregnancy.** (Die zusätzliche Prednisolon-Anwendung bei verschiedenen Tuberkulose-Verlaufsformen und während einer gleichzeitigen Schwangerschaft)
E. KUNTZ. *Beiträge zur Klinik der Tuberkulose und spezifischen Tuberkulose-Forschung* [*Beitr. Klin. Tuberk.*] **122**, 405–422, 1960. 8 figs., bibliography.

From the University Medical Clinic, Giessen, Germany, the author reports his experience with the addition of prednisolone to the therapy in 142 patients with various forms of tuberculosis. The 85 cases of pulmonary tuberculosis in the series included 30 chronic cases, 7 patients with miliary and 24 with active infiltrative disease; the remainder consisted of 4 cases of erythema nodosum, 17 of primary and 14 of secondary pleural effusion, 10 of tuberculous peritonitis, and 7 of tuberculous meningitis, while in 5 patients the lesions were confined to the bronchi. The prednisolone was given orally, except when marked vomiting made its intravenous administration necessary in the early stages. The initial daily dose ranging from 10 to 20 mg. was reduced by stages to 5 mg. daily, while the average total dose ranged from 281 mg. in erythema nodosum to 702 mg. in the chronic cases. Most of the other patients received between 400 and 500 mg. All patients were in addition receiving full doses of antituberculous drugs.

The best results, as indicated by more rapid clinical and radiological improvement, were obtained in the active and progressive pulmonary cases. All 7 patients with miliary tuberculosis became afebrile in a few days, and almost complete absorption of the miliary tubercles was achieved at the end of 6 weeks. Similar good results, without any permanent damage to the central nervous system, were obtained in the 7 cases of tuberculous meningitis, in which systemic therapy was reinforced by simultaneous intrathecal administration of prednisolone, streptomycin, and isoniazid. In 16 of the 30 chronic cases some improvement was noted, 9 of these patients becoming sputum-negative, in spite of having been harbouring previously proved resistant strains.

The author considers that miliary and caseous-pneumonic disease, pleural effusions, and meningitis are absolute indications for the institution of corticoid therapy, while he is of the opinion that this additional treatment should be considered in all severely toxic cases, in the presence of intercurrent complications such as asthma, hepatitis, or nephrosis, and in patients who have failed to respond to the usual chemotherapy. However, in view of the possible effects on the foetus during an associated pregnancy corticosteroids are advocated only in the most severe cases, and in no case should they be given for longer than 8 weeks, preferably between the 4th and 8th months of gestation. *H. F. Reichenfeld*

Tropical Diseases

462. **Medical Treatment of Mycetoma**
W. P. COCKSHOTT and A. M. RANKIN. *Lancet* [*Lancet*] **2**, 1112–1114, Nov. 19, 1960. 2 figs., 5 refs.

A plea is made for a more optimistic outlook in the treatment of mycetoma. A regime based on a short course of wide-spectrum antibiotic and prolonged treatment with dapsone by mouth has been found effective. In nearly half our cases, this treatment has avoided the need for amputation and enabled the patient to get back to work.—[Authors' summary.]

463. **The Pathology of Ocular Leprosy. I. Cornea**
J. H. ALLEN and J. L. BYERS. *Archives of Ophthalmology* [*Arch. Ophthal.*] **64**, 216–220, Aug., 1960. 3 refs.

The authors attempt to correlate the clinical findings with the pathological lesions in the eye in patients with leprosy. The specific leprotic lesions include opacity of the corneal nerves, avascular keratitis, and corneal lepromata. Opacification of the corneal nerves is a transitory lesion. The nerves appear as greyish-white, beaded lines extending from the periphery towards the centre of the cornea. The lesion is mainly oedematous but there is some cellular exudate which includes plasma cells and epithelioid cells containing bacilli. Foam cells are observed in older lesions. In avascular keratitis biomicroscopical examination reveals clusters of small, white opacities, which may be 0·25 to 0·5 mm. in diameter, in the superficial layers of the cornea. These "pearls" are miliary lepromata and are pathognomonic of the disease. Avascular keratitis is frequently asymptomatic and may develop and subside without the patient's knowledge, but it is always accompanied by iritis or uveitis. The cellular exudate in the lesion is at first polymorphonuclear, but this is quickly replaced by an exudate of plasma cells, lymphocytes, and epithelioid cells. The last develop into foam cells; these contain numerous bacilli in vacuoles, and sometimes coalesce to form giant cells. The cellular infiltrations occur in progressively deeper layers of the cornea spreading from the periphery to the centre. Pannus developing as a superficial vascularization may spread in from the superior temporal quadrant and then over the whole surface of the cornea. Vascular infiltration of the deeper layers of the cornea may follow or accompany the development of the superficial pannus and avascular keratitis. It may occur, however, without pannus in cases of severe leprotic uveitis. In the typical leprotic interstitial keratitis the capillaries grow in from the anterior scleral vessels. Acid-fast bacilli are found intracellularly in the cellular exudate, in endothelial cells, and in the pericellular stroma.

In the classification of lesions the authors recommend a simple code, using K for avascular keratitis, I.K. for interstitial keratitis, and P for pannus, with a 4-point grading of severity. They consider the beading of the corneal nerves to be the earliest sign of leprotic involvement of the eye, and that all leprologists should be trained to recognize this specific lesion which can be seen with a corneal loupe (at least ×8 magnification) or with the slit lamp and corneal microscope. *William Hughes*

464. **Clinical Trials with Entamide Furoate and Related Compounds. I. In a Non-tropical Environment**
A. W. WOODRUFF and S. BELL. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. roy. Soc. trop. Med. Hyg.*] **54**, 389–395, July, 1960.

In a non-tropical environment where reinfection can be discounted, three derivatives of dichloroace-4-hydroxy-N-methylanilide ("entamide"), the benzoate, piperazine sulphate, and the furoate have been tried in human infections with *Entamoeba histolytica*. Entamide benzoate, 40 mg. per kg. body weight daily for 10 days resulted in disappearance of parasites from the stools in an average of 3·6 days, and of 15 patients passing cysts who were followed-up after treatment there were two relapses. Entamide piperazine sulphate, 30 mg. per kg. body weight daily for 10 days resulted in disappearance of parasites from the stools in an average of 4 days, and of 14 chronically infected, treated and followed-up, one relapsed. Two patients having acute amoebic dysentery were treated, of whom one relapsed. Entamide furoate, 20 mg. per kg. body weight daily for 10 days resulted in disappearance of parasites from the stools in an average of 3·4 days, and of 30 in whose faeces cysts were present and who were followed-up after treatment one relapsed. Three patients with acute amoebic dysentery were treated of whom two followed-up did not relapse.—[Authors' summary.]

465. **Clinical Trials with Entamide Furoate, Entamide Piperazine Sulphate and Emetine Bismuth Iodide. II. In a Tropical Environment**
P. D. MARSDEN. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. roy. Soc. trop. Med.*] **54**, 396–399, July, 1960. 2 refs.

In this paper from the Hospital for Tropical Diseases, London, a comparative study is reported of the amoebicidal activity of furoate and piperazine sulphate derivatives of diloxanide ("entamide") and of emetine bismuth iodide, the field work being carried out in Nigeria. Patients were given emetine bismuth iodide in a dosage of 2 g. daily for 10 days or the furoate or the piperazine sulphate derivative of diloxanide in a dosage of 20 mg. per kg. body weight daily for 10 days.

Of 21 patients receiving emetine bismuth iodide 4 relapsed; of 55 treated with the piperazine sulphate derivative of diloxanide 14 relapsed, and of 71 given the furoate derivative 7 relapsed. In addition 16 patients in whom amoebic dysentery developed were treated with diloxanide furoate and 4 of these relapsed after treatment. No serious side-effects of the diloxanide compounds were encountered. *R. A. Neal*

Allergy

466. **Current Concepts of Etiology and Management in Otolaryngologic Allergy**
J. W. HAMPSEY. *Archives of Otolaryngology* [*Arch. Otolaryng.*] **72**, 21–24, July, 1960. 10 refs.

The author accepts the hypothesis of Godlowski and Sevag that a foreign protein entering a normal cell is hydrolyzed by the normal, non-specific proteinases. It is pointed out that if the enzyme proteolysis is not adequate the foreign protein is not completely hydrolyzed and either a new enzyme system is formed to deal with the intruder (this is the basis of acquired immunity) or a toxic enzyme system develops with "metabolic storms".

In allergy the aim of treatment is not to destroy the hypersensitive cells but to restore their normal function by administering a minimum dosage of antibodies. This applies to house-dust and pollen extracts, as well as to vaccines, histamine, and biological extracts. Food allergy is important. In some cases thyroid deficiency should be suspected, and the basal metabolic rate and, possibly, the serum protein-bound iodine level and thyroid iodine uptake should be determined. Corticosteroids are useful in some acute allergic attacks. Pregnancy may diminish attacks of hay-fever during the period of gestation, but may sometimes produce a vasomotor rhinitis. Hyperinsulinism due to excessive carbohydrate intake is often found in children and young adults with nasal symptoms resembling or mimicking allergic manifestations. A high-protein diet with low fat and low carbohydrate intake is needed to produce enzymes and reduce oedema. An adequate diet usually contains all needed minerals and vitamins, but during active periods of the disease supplementary vitamins may help, such as ascorbic acid, which is necessary for proper functioning of the adrenal cortex, and α-tocopherol, which has an antihyaluronidase factor that helps to reduce the spread of inflammation. Pantothenic acid and pyridoxine are also valuable.

F. W. Watkyn-Thomas

467. **The Effect of Antiserotonin (Cyproheptadine) and Antihistamine on Cutaneous Allergy.** [In English]
K. JENSEN. *Acta allergologica* [*Acta allerg.* (*Kbh.*)] **15**, 293–305, 1960. 4 figs., 20 refs.

It is not known whether serotonin plays an important part in allergic reactions in man, but it has properties similar to those of histamine and is present in the blood in larger amounts in an allergic subject than in a non-allergic one.

In a study at the University Clinic, Copenhagen, the effect of an antiserotonin substance, cyproheptadine (1 - methyl - 4 - (5 - dibenzo - [a:*e*] - cycloheptatri - enylidene)-piperidine hydrochloride monohydrate) was compared with that of the antihistamine preparation thephorin in patients with seasonal hay-fever. A total of 112 such patients were divided into 6 groups, all being tested with grass-pollen extract in four concentrations and histamine in three concentrations. In 5 of the groups varying doses of cyproheptadine and thephorin were then given; the sixth group received no drugs. After one week's treatment the patients were again tested with the same concentrations of pollen extract and histamine.

The drug, which pharmacologically and physiologically had a strong antagonistic serotonin effect, also had an antagonistic effect on pollen and histamine reactions. This effect was evident after a dose of 2·5 mg. daily. Side-effects were similar to those of antihistaminic drugs in that drowsiness and sluggishness were observed in some patients and one had dryness of the mucous membranes. As the author points out it is impossible from these results to determine whether serotonin is significant in allergic reactions in man.

A. W. Frankland

468. ***In-vitro* Fixation of Skin-sensitizing Antibodies to Skin Cells and Mesenchymal Tissue.** [In English]
T. SAMSØE-JENSEN and K. HAUGE-KRISTENSEN. *Acta allergologica* [*Acta allerg.* (*Kbh.*)] **15**, 202–207, 1960. 6 refs.

A solution of serum containing skin-sensitizing antibodies was incubated *in vitro* with skin (untreated, treated with cold, and heated), muscle fascia, and peritoneal connective tissue. Subsequent passive transfer reactions by the method of Prausnitz–Küstner appeared to indicate *in vitro* fixation of the antibodies to untreated and frozen skin. No fixation occurred to heated skin (denaturation of protein?) or to mesenchymal tissue, such as muscle fascia and peritoneal connective tissue. —[Authors' summary.]

469. **Investigations of Spontaneous Hypersensitivity of the Dog**
R. PATTERSON. *Journal of Allergy* [*J. Allergy*] **31**, 351–363, July–Aug., 1960. 10 figs., 15 refs.

In this experimental study carried out at the University of Michigan Medical School, Ann Arbor, a ragweed-sensitive dog was enclosed in a chamber and exposed to various concentrations of ragwood pollen suspensions in water which were delivered into the chamber by means of a nebulizer. Respiration was recorded by a stethograph. When asthmatic attacks were caused by daily exposure to ragweed pollen the sensitivity of the dog gradually decreased, but increased again when the intervals between exposures were lengthened. An aerosol of 1·5% serotonin did not cause an asthmatic response, and lysergic acid diethyamide (LSD) did not modify the pollen-produced asthmatic attack. The administration of adrenaline, however, had the expected antiasthmatic effect.

H. Herxheimer

Gastroenterology

470. Acute Hemorrhagic Necrosis of the Gastro-intestinal Tract

SI-CHUN MING and R. LEVITAN. *New England Journal of Medicine* [*New Engl. J. Med.*] **263**, 59–65, July 14, 1960. 3 figs., 19 refs.

Acute haemorrhagic necrosis of the gastro-intestinal tract was first described under the term " acute haemorrhagic enterocolitis " by Wilson and Qualheim (*Gastroenterology*, 1954, **27**, 431; *Abstr. Wld Med.*, 1955, **17**, 374). The present authors found 11 cases of this condition among 698 on which necropsy was performed at Beth Israel Hospital, Boston. Describing the clinical features in these 11 cases they state that most of the patients were elderly and chronically ill, 8 having long-standing congestive cardiac failure, associated in 4 with acute complications such as myocardial infarction and subacute bacterial endocarditis. Of the remaining 3 patients, one had arteriosclerotic gangrene, one acute peritonitis secondary to cholecystitis, and one hypertension and cardiac arrhythmia. The onset of the illness was sudden, and in 4 patients shock was the only clinical manifestation. Gastro-intestinal haemorrhage was obvious in 6, being severe in 2. In general, the abdominal signs were indefinite, in contrast to the signs in other acute abdominal conditions. The clinical course of the illness was short, the patients dying rapidly in irreversible shock.

At necropsy there was involvement of all parts of the alimentary tract (except the oesophagus), the small intestine, especially the ileum, being affected in all cases. The lesions were commonly multiple and extensive. The mucosa and sometimes also the submucosa were dark purplish red and contained obvious haemorrhage and oedema. Small, shallow ulcers were seen in 4 cases. Bloody fluid was often present in the gut. Histologically, the mucosa was haemorrhagic, the villi were oedematous and blunted, with necrotic tips, the vessels of the mucosa and submucosa were dilated and engorged, but the muscular coats and serosa were virtually normal. There was no evidence in any of the cases of thrombi or inflammation.

The authors emphasize that the clinical manifestations, apart from shock, may be insignificant, so that the condition is often not diagnosed during life. The cause is unknown. There was no evidence in the series of any toxic reaction to the mercurial diuretics given in the treatment of heart failure, of a Shwartzman reaction, of ulcerative colitis, or of vascular occlusion. The authors consider that the shock is not necessarily due to the blood loss and that it appears to be irreversible.

A. Gordon Beckett

471. Gastric Cytodiagnosis: a Review and Appraisal

D. D. GIBBS. *Gut* [*Gut*] **1**, 205–216, Sept., 1960. 24 figs., 17 refs.

472. Increased Incidence of Peptic Ulcer in Patients with Emphysema. (Zur Ulcushäufung beim Emphysem)

W. HEGETSCHWEILER, A. HUNZIKER, and E. MARANTA. *Schweizerische medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **90**, 1012–1016, Sept. 3, 1960. 37 refs.

Following the death at the University Medical Clinic, Zürich, of 2 emphysematous patients from profuse haematemesis as the result of peptic ulcer the authors decided to re-evaluate the impression they had gained from the recent literature that peptic ulcer occurs more commonly in emphysematous patients than in the general population. The study was based on the records of 6,077 patients over 16 years of age seen during 1958–9, representing every variety of medical condition dealt with at the Clinic. In 90 women and 209 men a diagnosis of peptic ulcer was established beyond possible doubt, while in 51 women and 250 men emphysema was diagnosed only after critical examination of the history, clinical and radiological findings, and exhaustive tests of pulmonary function. In this latter group peptic ulcer was not found in any of the 51 women, but was present in 26 (10·4%) of the 250 men. In 10 cases the first evidence of the ulcer was haemorrhage, in one it was its perforation, while in 5 further unsuspected cases it was discovered radiologically or at necropsy. In a small control group of 35 patients with pulmonary disease other than emphysema, peptic ulcer was present in 2.

The authors consider that the incidence of peptic ulcer in emphysematous males is not only statistically important, but that its occurrence rate rises with the severity of the pulmonary lesion. Because the ulcer tends to be silent and to lead in some cases to catastrophic complications, it should be diligently sought for in every case. In discussing the pathogenesis the authors refer to the psychosomatic nature of both diseases. They did not find smoking to be an exogenous factor, and they regard hypercapnia and hypoxia as of doubtful significance. None of their emphysematous patients had received steroid therapy which, with other therapeutic measures in emphysema, may lead to the production of peptic ulcer.

E. S. Wyder

473. Colloid Osmotic Pressure and Hydrostatic Pressure Relationships in the Formation of Ascites in Hepatic Cirrhosis

G. R. CHERRICK, D. N. S. KERR, A. E. READ, and S. SHERLOCK. *Clinical Science* [*Clin. Sci.*] **19**, 361–375, Aug., 1960. 5 figs., 39 refs.

The formation of ascites in patients with cirrhosis of the liver is usually explained in terms of the Starling equilibrium, the net hydrostatic pressure across the portal capillary walls (" effective portal pressure ") being opposed by the colloid osmotic pressure difference between plasma and ascitic fluid (" effective colloid osmotic pressure "). The authors, working at the Postgraduate

Allergy

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In allergy the aim of treatment is not to destroy the hypersensitive cells but to restore their normal function by administering a minimum dosage of antibodies. This applies to house-dust and pollen extracts, as well as to vaccines, histamine, and biological extracts. Food allergy is important. In some cases thyroid deficiency should be suspected, and the basal metabolic rate and, possibly, the serum protein-bound iodine level and thyroid iodine uptake should be determined. Corticosteroids are useful in some acute allergic attacks. Pregnancy may diminish attacks of hay-fever during the period of gestation, but may sometimes produce a vasomotor rhinitis. Hyperinsulinism due to excessive carbohydrate intake is often found in children and young adults with nasal symptoms resembling or mimicking allergic manifestations. A high-protein diet with low fat and low carbohydrate intake is needed to produce enzymes and reduce oedema. An adequate diet usually contains all needed minerals and vitamins, but during active periods of the disease supplementary vitamins may help, such as ascorbic acid, which is necessary for proper functioning of the adrenal cortex, and α-tocopherol, which has an antihyaluronidase factor that helps to reduce the spread of inflammation. Pantothenic acid and pyridoxine are also valuable.

F. W. Watkyn-Thomas

467. **The Effect of Antiserotonin (Cyproheptadine) and Antihistamine on Cutaneous Allergy.** [In English]
K. JENSEN. *Acta allergologica* [*Acta allerg.* (*Kbh.*)] **15**, 293–305, 1960. 4 figs., 20 refs.

It is not known whether serotonin plays an important part in allergic reactions in man, but it has properties similar to those of histamine and is present in the blood in larger amounts in an allergic subject than in a non-allergic one.

In a study at the University Clinic, Copenhagen, the effect of an antiserotonin substance, cyproheptadine (1 - methyl - 4 - (5 - dibenzo - [a:*e*] - cycloheptatri - enylidene)-piperidine hydrochloride monohydrate) was compared with that of the antihistamine preparation thephorin in patients with seasonal hay-fever. A total of 112 such patients were divided into 6 groups, all being tested with grass-pollen extract in four concentrations and histamine in three concentrations. In 5 of the groups varying doses of cyproheptadine and thephorin were then given; the sixth group received no drugs. After one week's treatment the patients were again tested with the same concentrations of pollen extract and histamine.

The drug, which pharmacologically and physiologically had a strong antagonistic serotonin effect, also had an antagonistic effect on pollen and histamine reactions. This effect was evident after a dose of 2·5 mg. daily. Side-effects were similar to those of antihistaminic drugs in that drowsiness and sluggishness were observed in some patients and one had dryness of the mucous membranes. As the author points out it is impossible from these results to determine whether serotonin is significant in allergic reactions in man.

A. W. Frankland

468. ***In-vitro* Fixation of Skin-sensitizing Antibodies to Skin Cells and Mesenchymal Tissue.** [In English]
T. SAMSØE-JENSEN and K. HAUGE-KRISTENSEN. *Acta allergologica* [*Acta allerg.* (*Kbh.*)] **15**, 202–207, 1960. 6 refs.

A solution of serum containing skin-sensitizing antibodies was incubated *in vitro* with skin (untreated, treated with cold, and heated), muscle fascia, and peritoneal connective tissue. Subsequent passive transfer reactions by the method of Prausnitz–Küstner appeared to indicate *in vitro* fixation of the antibodies to untreated and frozen skin. No fixation occurred to heated skin (denaturation of protein?) or to mesenchymal tissue, such as muscle fascia and peritoneal connective tissue. —[Authors' summary.]

469. **Investigations of Spontaneous Hypersensitivity of the Dog**
R. PATTERSON. *Journal of Allergy* [*J. Allergy*] **31**, 351–363, July–Aug., 1960. 10 figs., 15 refs.

In this experimental study carried out at the University of Michigan Medical School, Ann Arbor, a ragweed-sensitive dog was enclosed in a chamber and exposed to various concentrations of ragwood pollen suspensions in water which were delivered into the chamber by means of a nebulizer. Respiration was recorded by a stethograph. When asthmatic attacks were caused by daily exposure to ragweed pollen the sensitivity of the dog gradually decreased, but increased again when the intervals between exposures were lengthened. An aerosol of 1·5% serotonin did not cause an asthmatic response, and lysergic acid diethyamide (LSD) did not modify the pollen-produced asthmatic attack. The administration of adrenaline, however, had the expected antiasthmatic effect.

H. Herxheimer

Gastroenterology

470. Acute Hemorrhagic Necrosis of the Gastro-intestinal Tract

SI-CHUN MING and R. LEVITAN. *New England Journal of Medicine* [*New Engl. J. Med.*] **263**, 59–65, July 14, 1960. 3 figs., 19 refs.

Acute haemorrhagic necrosis of the gastro-intestinal tract was first described under the term " acute haemorrhagic enterocolitis " by Wilson and Qualheim (*Gastroenterology*, 1954, **27**, 431; *Abstr. Wld Med.*, 1955, **17**, 374). The present authors found 11 cases of this condition among 698 on which necropsy was performed at Beth Israel Hospital, Boston. Describing the clinical features in these 11 cases they state that most of the patients were elderly and chronically ill, 8 having long-standing congestive cardiac failure, associated in 4 with acute complications such as myocardial infarction and subacute bacterial endocarditis. Of the remaining 3 patients, one had arteriosclerotic gangrene, one acute peritonitis secondary to cholecystitis, and one hypertension and cardiac arrhythmia. The onset of the illness was sudden, and in 4 patients shock was the only clinical manifestation. Gastro-intestinal haemorrhage was obvious in 6, being severe in 2. In general, the abdominal signs were indefinite, in contrast to the signs in other acute abdominal conditions. The clinical course of the illness was short, the patients dying rapidly in irreversible shock.

At necropsy there was involvement of all parts of the alimentary tract (except the oesophagus), the small intestine, especially the ileum, being affected in all cases. The lesions were commonly multiple and extensive. The mucosa and sometimes also the submucosa were dark purplish red and contained obvious haemorrhage and oedema. Small, shallow ulcers were seen in 4 cases. Bloody fluid was often present in the gut. Histologically, the mucosa was haemorrhagic, the villi were oedematous and blunted, with necrotic tips, the vessels of the mucosa and submucosa were dilated and engorged, but the muscular coats and serosa were virtually normal. There was no evidence in any of the cases of thrombi or inflammation.

The authors emphasize that the clinical manifestations, apart from shock, may be insignificant, so that the condition is often not diagnosed during life. The cause is unknown. There was no evidence in the series of any toxic reaction to the mercurial diuretics given in the treatment of heart failure, of a Shwartzman reaction, of ulcerative colitis, or of vascular occlusion. The authors consider that the shock is not necessarily due to the blood loss and that it appears to be irreversible.

A. Gordon Beckett

471. Gastric Cytodiagnosis: a Review and Appraisal

D. D. GIBBS. *Gut* [*Gut*] **1**, 205–216, Sept., 1960. 24 figs., 17 refs.

472. Increased Incidence of Peptic Ulcer in Patients with Emphysema. (Zur Ulcushäufung beim Emphysem)

W. HEGETSCHWEILER, A. HUNZIKER, and E. MARANTA. *Schweizerische medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **90**, 1012–1016, Sept. 3, 1960. 37 refs.

Following the death at the University Medical Clinic, Zürich, of 2 emphysematous patients from profuse haematemesis as the result of peptic ulcer the authors decided to re-evaluate the impression they had gained from the recent literature that peptic ulcer occurs more commonly in emphysematous patients than in the general population. The study was based on the records of 6,077 patients over 16 years of age seen during 1958–9, representing every variety of medical condition dealt with at the Clinic. In 90 women and 209 men a diagnosis of peptic ulcer was established beyond possible doubt, while in 51 women and 250 men emphysema was diagnosed only after critical examination of the history, clinical and radiological findings, and exhaustive tests of pulmonary function. In this latter group peptic ulcer was not found in any of the 51 women, but was present in 26 (10·4%) of the 250 men. In 10 cases the first evidence of the ulcer was haemorrhage, in one it was its perforation, while in 5 further unsuspected cases it was discovered radiologically or at necropsy. In a small control group of 35 patients with pulmonary disease other than emphysema, peptic ulcer was present in 2.

The authors consider that the incidence of peptic ulcer in emphysematous males is not only statistically important, but that its occurrence rate rises with the severity of the pulmonary lesion. Because the ulcer tends to be silent and to lead in some cases to catastrophic complications, it should be diligently sought for in every case. In discussing the pathogenesis the authors refer to the psychosomatic nature of both diseases. They did not find smoking to be an exogenous factor, and they regard hypercapnia and hypoxia as of doubtful significance. None of their emphysematous patients had received steroid therapy which, with other therapeutic measures in emphysema, may lead to the production of peptic ulcer.

E. S. Wyder

473. Colloid Osmotic Pressure and Hydrostatic Pressure Relationships in the Formation of Ascites in Hepatic Cirrhosis

G. R. CHERRICK, D. N. S. KERR, A. E. READ, and S. SHERLOCK. *Clinical Science* [*Clin. Sci.*] **19**, 361–375, Aug., 1960. 5 figs., 39 refs.

The formation of ascites in patients with cirrhosis of the liver is usually explained in terms of the Starling equilibrium, the net hydrostatic pressure across the portal capillary walls (" effective portal pressure ") being opposed by the colloid osmotic pressure difference between plasma and ascitic fluid (" effective colloid osmotic pressure "). The authors, working at the Postgraduate

Medical School of London, measured all 4 factors concerned in this equilibrium in 11 patients with ascites. Colloid osmotic pressures were measured with an electronic colloid osmometer and the effective portal pressure was obtained by subtracting the intra-abdominal pressure from the intrasplenic pressure, both of which were measured directly by puncture of the lateral abdominal wall. The intrasplenic pressure and plasma colloid osmotic pressure were also determined in 35 patients with cirrhosis of the liver without ascites. The mean intrasplenic pressure was higher in the patients with ascites, but the effective portal pressure did not differ significantly in the two groups. The effective colloid osmotic pressure in every patient with ascites was less than the lowest colloid osmotic pressure found in any patient without ascites. The implications of these findings are discussed.

P. C. Reynell

474. **A Chemical and Bacteriological Study of Gall-Stones. The Presence of an Actinomycete**
A. J. H. Rains, G. J. Barson, N. Crawford, and J. F. D. Shrewsbury. *Lancet* [*Lancet*] **2**, 614–618, Sept. 17, 1960. 2 figs., 19 refs.

The early theories, chemical and bacteriological, of the cause of gallstone formation are outlined. Research into the reproducibility of previous findings, as part of a wider programme of investigations, led to a study of whole and central portions of 57 specimens of gallstones by qualitative chemical analysis and the bacteriological methods of direct smear, culture and serology.

An *Actinomyces* was isolated from 30 of the 57 specimens. The serological character of each organism indicates the presence of a species distinct from *Actinomyces bovis*. The findings of previous investigators were not confirmed and a possible explanation is given. Chemical analysis did not confirm any dominance of cholesterol or bile-pigment especially in the centre of the stones and shows that protein and carbonate deserve as much attention. There is no apparent difference in the stones that did and did not grow *Actinomyces*. The old theory of blood-borne infection causing a gall-bladder lesion and calculus formation from a distant focus, such as the mouth, is reintroduced with reference to a species of *Actinomyces* found in oral concrements.

An indication is given of the uses of serology and bacteriological chemistry (with respect to protein and inorganic constituents) in the furtherance of such research.—[Authors' summary.]

475. **The Contractility of the Gall-bladder in Health and in the Presence of Gastric and Duodenal Ulcer.** (Рентгенологические показатели моторно-эвакуаторной деятельности желчного пузыря у здоровых людей и при язвенной болезни желудка и двенадцатиперстной кишки)
G. D. Golub. *Вестник Рентгенологии и Радиологии* [*Vestn. Rentgenol. Radiol.*] **35**, 17–21, Sept.–Oct., 1960. 3 figs., 8 refs.

The contractility of the gall-bladder was studied in 20 healthy individuals and in 123 patients suffering from either gastric or duodenal ulcer, the contraction of the opacified gall-bladder being initiated by the ingestion of two raw egg-yolks. Cholecystography was also carried out on 4 dogs by a special method developed by the author.

The state of contraction of the gall-bladder was found to last for 1½ to 2¼ hours and was followed by relaxation. The greater part of the contraction occurred in the first 30 minutes, during which time the gall-bladder lost between 60 and 85% of its original bile content. The author states that retention of a certain proportion of bile in the gall-bladder is quite normal and that the proportion retained varies according to the number of egg-yolks ingested. Hyper- or hypo-kinesis of the gall-bladder was observed in patients suffering from gastric or duodenal ulcer, being particularly marked in the latter condition, but the degree of dyskinesia depended on the site of the ulcer.

A. Orley

476. **Fulminant Ulcerative Colitis**
J. G. Rankin, S. J. M. Goulston, R. W. Boden, and A. W. Morrow. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **29**, 375–390, July [received Sept.], 1960. 13 figs., 40 refs.

Of 190 consecutive patients with ulcerative colitis seen at the Royal Prince Alfred Hospital, Sydney, between 1950 and 1958, 22 had the fulminating form of the disease. The fulminating episodes were the first manifestations of colitis in 9 of the patients; in the remainder there was a fulminant relapse of colitis which had been present for periods varying from a few months to 19 years with, usually, long periods of remission. Precipitating psychological factors were evident in 7 of the patients.

The onset of the episodes was more sudden in patients in relapse than in those with initial fulminant disease. Diarrhoea was often extremely severe, with considerable blood in the stools in all except 5 patients. Neutrophil leucocytosis, with a marked shift to the left, was almost always present, but there was no definite relationship between the total leucocyte count or the neutrophil distribution and the presence of perforation or peritonitis. Perforation occurred in 4 patients, all of whom had received corticosteroids. Peritonitis, which proved fatal, was seen only in 4 patients in relapse; in one of these there was no obvious perforation. Marked dilatation of the colon, frequently segmental and proximal to the splenic flexure, was noted in 9 patients, 2 of whom recovered without surgery. The dilatation was not always at the site of maximal ulceration; in those cases in which histological examination was possible no evidence of ganglionic degeneration was observed at the site of dilatation. In one patient, who had not received steroids, acute adrenal insufficiency developed after operation, and in another, who had been given steroids, there was evidence at necropsy of necrosis of the adrenal gland. Skin lesions, which were noted in 9 patients, were more frequent than is generally the case in colitis. Pulmonary complications were responsible for 5 deaths in the series, 4 from thrombosis or embolism of the pulmonary artery and one from bilateral pulmonary collapse. A further patient had a severe staphylococcal infection. Mortality

in the series was high; of 7 patients treated medically 2 died and of 15 subjected to operation 9 died. Only 2 of the 10 patients given steroids improved, 8 remaining unchanged or becoming worse. At necropsy severe fatty changes in the liver were noted in 4 cases and periportal cholangiitis in one.

The authors stress that initial fulminant colitis may be difficult to diagnose in the absence of blood in the stool, but invariably toxaemia and loss of weight, sometimes severe, are present. Normal appearances on barium-enema examination do not exclude a diagnosis of ulcerative colitis. In the treatment of this type of colitis steroids are of limited value, rarely producing remission and more often [but the evidence for this is not convincing] complicating management, causing progression of the disease, delaying operation, masking symptoms, giving rise to complications, and increasing the incidence and severity of postoperative complications.

The authors also emphasize the danger of delaying surgery, and recommend full supportive measures for a maximum period of 2 weeks and then, if the improvement is not sufficient, surgery in the form of ileostomy and subtotal colectomy. As a preoperative precaution broad spectrum antibiotics should be given by injection and sometimes also by mouth, administration of steroids being restricted to those patients who had had them previously. *A. Gordon Beckett*

477. **Chronic Ulcerative Colitis: a Clinical Appraisal and Follow-up Study**

A. E. LINDNER, R. C. KING, and R. J. BOLT. *Gastroenterology* [*Gastroenterology*] **39**, 153–160, Aug., 1960. 15 refs.

The authors have reviewed the records of all (391) patients with ulcerative colitis treated at the University of Michigan Hospital, Ann Arbor, between 1947 and 1956 and in whom there was sigmoidoscopic, radiological, or pathological confirmation of the diagnosis. The sex distribution was approximately equal, 53% of the patients being male. In 250 cases the first symptoms developed in the second and third decades of life. Barium enema examination in 359 cases revealed involvement of the whole colon in 45%, left-sided changes in 12%, lesions of the sigmoid colon only in 14%, of the right colon only in 4%, and no abnormality in 26%; the terminal ileum was affected in 12%. Pseudopolypi were identified in 100 patients by means of sigmoidoscopy, radiological examination, or histological study. There were 29 deaths in hospital and 15 patients underwent total procto-colectomy.

In 1959 virtually all the remaining patients (342 out of 347) were followed up by means of a questionary. The replies to this, together with the hospital records, revealed that 61 (16%) of the 386 patients had died and 107 (33%) of the remainder had received some type of surgical treatment. The pathological reports, which were available for 93 of the 95 patients who had undergone resection and for one-third of those who had died, recorded 8 cases of carcinoma, all but one of these occurring in men. Although only 43% of the whole group had had ulcerative colitis for 10 years or more this fraction included 7 of the 8 patients with carcinoma, so that the incidence of carcinoma in this group was 4·3%. Carcinoma was found in 8 (6·9%) of 116 pathological specimens examined. It had presented as an abdominal mass in one case, as a pelvic mass in one, was discovered at operation for ileo-colic fistula and perforation respectively in 2 cases, was suggested by unexplained anaemia in one patient, while it was found unexpectedly at necropsy in the remaining 3. Information regarding the severity of the disease, which was available for 312 patients, showed that at the time of follow-up 42% had only mild symptoms, 30% had moderately severe symptoms or required conservative medical treatment, 7% had severe symptoms, and 20% had died or had other systemic disease. In conclusion the authors point out that disease lasting over 15 years and starting before the age of 20 carried an increased risk of carcinoma. The problem of whether or not to perform prophylactic colectomy rarely arose in this series since most of these patients required colectomy because of the severity of their disease. *G. L. Asherson*

478. **Inhibitory Effect of New Anticholinergics on the Basal and Secretin-stimulated Pancreatic Secretion in Patients with and without Pancreatic Disease. Therapeutic and Theoretic Implications**

D. A. DREILING and H. D. JANOWITZ. *American Journal of Digestive Diseases* [*Amer. J. dig. Dis.*] **5**, 639–654, July, 1960. 2 figs., 28 refs.

At the Mount Sinai Hospital, New York, the effect on pancreatic secretion of four piperidyl anticholinergic drugs was compared with that of atropine and "banthine" (methanthaline bromide). Pipenzolate methobromide ("piptal") and "cantil" (N-methyl-3-piperidyl-diphenylglycolate methobromide) proved to be the most potent inhibitors; less effective were "dactyl" (N - ethyl - 3 - piperidyl - diphenylacetate hydrochloride and 1 - phenyl - 1 - (2 thienyl) - 4 - diethylamino - 2 - butyn-1-ol methylbromide).

Inhibition of volume flow and bicarbonate and enzyme secretion was much greater (approximately 30 to 40%) than in patients given atropine or banthine and its derivatives, this being observed in patients without pancreatic disease as well as in those with pancreatitis and in both basal and secretin-stimulated secretion. Volume and bicarbonate secretory responses were depressed by about 80% and enzyme production by about 95% by dosages just below those at which side-reactions appeared. At the dose ranges studied the anticholinergic agents completely suppressed gastric secretion, a finding which should be helpful in the management of both acute and chronic pancreatitis.

The results suggest that the hormonal and nervous mechanisms may be interdependent in regulating pancreatic secretion, and that the persistence of bicarbonate concentration at falling rates of secretion after administration of anticholinergic drugs, acetazolamide, ACTH (corticotrophin), or steroids favours the hypothesis of ductular function within the pancreas.

Guy Blackburn

Cardiovascular System

479. **Atheroma and Saturation of Depôt Fat**
H. G. PENMAN. *Clinical Science* [*Clin. Sci.*] **19**, 435–438, Aug., 1960. 2 figs., 11 refs.

Of the various possible aetiological factors in atheroma fat intake and the quality of dietary fat have lately been extensively studied. There is evidence that the quality of dietary fat may influence the constitution of the fat depots as measured by their iodine number. At St. Thomas's Hospital Medical School, London, an investigation was carried out to determine the relationship, if any, between the iodine number of the subcutaneous fat and the presence of atheroma. At necropsy on 50 subjects 3 g. of subcutaneous fat was taken in each case from the anterior abdominal wall and the individual iodine number determined. The degree of atheroma was graded on a 4-point scale. The mean iodine number for these 50 cases closely corresponded to the figure given in textbooks. There was no significant difference between the average iodine number for patients with severe coronary disease and those with minimal or severe atheroma.

Thus, no definite evidence could be found that severe aortic atheroma or coronary arterial disease was in any way associated with highly saturated subcutaneous fat.
Z. A. Leitner

480. **Hypothermia and the Heart–Lung Machine: Clinical Application of the Technique**
D. N. ROSS. *British Medical Journal* [*Brit. med. J.*] **2**, 571–572, Aug. 20, 1960. 4 figs., 4 refs.

Experience of the use of hypothermia in combination with a heart–lung machine is reported in this paper from Guy's Hospital, London. The priming volume of the apparatus, a modification of the Kay–Cross oxygenator, is about 3 pints (1·7 litres). Cooling begins as soon as partial heart by-pass starts; at about 30° C., when the metabolic requirements are reduced to about 50% and the required blood flow is correspondingly reduced, full by-pass is instituted, and the patient's temperature reduced still further. In cases of complicated defects requiring a long period of by-pass, or of calcified aortic stenosis in which it is necessary to cross-clamp the aorta to provide a dry operative field (with a consequent interruption of coronary blood flow), the temperature is reduced to 17 to 20° C.

This technique has been used in 25 patients aged 2 to 47 years. Of the 6 deaths 4 occurred in bad-risk patients.
R. L. Hurt

481. **A-V Nodal Parasystole**
D. SCHERF, C. BORNEMANN, and M. YILDIZ. *American Heart Journal* [*Amer. Heart J.*] **60**, 179–187, Aug., 1960. 5 figs., 10 refs.

Parasystole arising in the atrio-ventricular (A–V) node is a rare form of cardiac arrhythmia. In this paper from New York Medical College 4 cases are described which were seen over a period of 14 months. In 3 of the patients, whose ages ranged from 58 to 73 years, there was evidence of ischaemic heart disease.

In each, an independently acting pacemaker was presumed to be present in the A–V node initiating beats with a regular rhythm and a rate rather slower than that of the sino-auricular (S–A) node. Many of the ectopically arising stimuli fell in the refractory period, but when they did initiate beats these occurred at various points in diastole and had a low upright P wave in Lead 1 and deeply inverted P wave in Leads 2 and 3. If occurring late in diastole, atrial "combination beats" due to simultaneous antegrade activation from the S–A node and retrograde activation from the ectopic focus were seen. Ventricular complexes had the same form in ectopic beats as in normal ones. *J. A. Cosh*

482. **Natural History of *Streptococcus faecalis* Endocarditis**
C. C. S. TOH and K. P. BALL. *British Medical Journal* [*Brit. med. J.*] **2**, 640–644, Aug. 27, 1960. 22 refs.

Of a total of 49 proved cases of bacterial endocarditis admitted to the Central Middlesex Hospital, London, in a recent 9-year period the infection in 8 was due to *Streptococcus faecalis*; in addition one patient had bacterial endarteritis due to this organism. The ages of the patients (5 male and 4 female) ranged from 20 to 77 years. There were signs of mitral valve disease in 4 cases, accompanied in 3 by signs of aortic stenosis or incompetence; in the remaining 5 patients no evidence of any underlying cardiac lesion was found. The infection followed operations or infections of the genito-urinary tract in 3 cases, a liver abscess in one case, and was associated with septic teeth in 3. No focus of infection was found in the remaining 2 cases.

Death occurred from congestive cardiac failure in 3 patients and from cerebral haemorrhage in a fourth. Prolonged treatment with massive doses of penicillin (2 to 16 mega units daily) and streptomycin (1 to 4 g. daily) seemed to give better results than tetracycline therapy, even in the absence of sensitivity *in vitro*. Eighth-nerve damage due to streptomycin, which was accepted as a calculated risk in view of the poor prognosis in the condition, developed in 4 patients. *H. F. Reichenfeld*

483. **Myocardial Necrosis following Elective Cardiac Arrest Induced with Potassium Citrate**
J. A. MCFARLAND, L. B. THOMAS, J. W. GILBERT, and A. G. MORROW. *Journal of Thoracic and Cardiovascular Surgery* [*J. thorac. cardiovasc. Surg.*] **40**, 200–208, Aug., 1960. 6 figs., 8 refs.

In open cardiac operations with cardiopulmonary bypass wide use has been made of Melrose's technique, in which the heart is arrested by the injection of potassium citrate solution into the ascending aorta proximal to an

occluding clamp. The authors, working at the Clinic of Surgery, National Heart Institute, Bethesda, Maryland, found that after arrest there was difficulty in some cases in re-establishing effective myocardial contraction and that an occasional patient showed evidence of left ventricular failure. This prompted a study of the hearts of 30 patients who had died at various intervals after direct-vision intracardiac operations, 19 of whom had been subjected to cardiac arrest induced with potassium citrate. Of the remaining 11 patients no form of arrest was attempted in 9, while arrest was induced in 2 by aortic occlusion alone. In all cases a total cardio-respiratory by-pass was provided.

In 15 of the 19 patients subjected to potassium citrate arrest, but not in any of the 11 in which this was not carried out, a distinctive type of necrosis was observed in various portions of the myocardium. It consisted of multiple, sharply circumscribed, microscopic areas of necrosis varying in number and usually in the central part of the myocardium. The necrotic fibres were swollen and stained intensely with eosin. Absence of haemorrhage or congestion was striking. The extent varied from single microscopic areas to massive necrosis and was more severe in the left ventricle. Thrombosis or necrosis of the coronary arteries was not observed to be associated with the lesions. The occurrence and severity of the lesions was not correlated with the amount of salt perfused, duration of perfusion, or duration of cardiac arrest. The authors conclude that myocardial necrosis is unequivocally associated with perfusion of the heart with potassium citrate and more likely to occur if the solution is freshly prepared from crystals.

Similar lesions have been found experimentally in animals after cardiac arrest with potassium citrate. Clinically, the condition may show itself as a gradually progressive hypotension which becomes unresponsive to pressor agents and is accompanied by rising venous pressure. These observations have led to the abandonment of potassium citrate infusion to induce cardiac arrest at the National Heart Institute.

R. Wyburn-Mason

484. **Embolic Occlusion of the Aorta in Patients with Mitral Stenosis**

A. E. A. Read, K. P. Ball, and C. G. Rob. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **29**, 459–471, July [received Sept.], 1960. 3 figs., 26 refs.

The degree of obstruction to the circulation resulting from arterial embolism may depend on the interplay of five factors—namely, the plugging effect of the embolus, migration of the embolus, extent of secondary thrombosis, the presence of arterial spasm, and the effectiveness of the collateral circulation. In this paper from the Central Middlesex and St. Mary's Hospitals, London, 22 cases of aortic embolic obstruction with mitral stenosis and auricular fibrillation are described. In 9 of the 22 patients (18 female and 4 male, aged 36 to 54 years) there were classic symptoms with acute, catastrophic onset. Of the 3 who survived in this group, all retained good peripheral circulation, one after conservative treatment, one after femoral embolectomy at 2 hours, and one after aortic embolectomy at 5 hours. Aortic embolectomy was performed in 6 patients and femoral embolectomy in 2. Further embolism caused 5 of the deaths in this group.

Subacute or insidious occlusion occurred in 12 patients, in 9 of whom the condition was diagnosed only in retrospect. In some of the patients in this group there was a sudden onset of pain in the lower abdomen, buttocks, or legs, with coldness, paraesthesiae, and muscular weakness. In the remaining patient in the series signs of aortic occlusion developed, but these disappeared within a few hours.

The authors state that the end-result of aortic embolectomy is often disappointing but that spontaneous recovery does occur in cases with subacute onset. After the cardiac condition has been controlled active medical treatment of the embolism should be started, including absolute rest, administration of morphine or pethidine, exposure of the legs (which should be level or slightly dependent), reflex heating of the body and upper limbs with, possibly, an indwelling caudal catheter for injection of 0·5% lignocaine, and administration of heparin (pending a decision about operation) and of alcohol for vasodilatation. If sensation, power, and warmth do not return to the feet embolectomy should not be delayed; this should be followed by anticoagulant therapy indefinitely or until mitral valvotomy can be performed. Arterial grafting should be considered for patients with severe claudication.

Of 16 patients who survived the acute attack 9 were alive from 6 months to 7 years later (average 3½ years), 4 died after 8 months to 4 years (average 2¼ years), and 3 were not traced.

R. S. Stevens

DIAGNOSTIC METHODS

485. **Radioiodine Uptake by the Infarcted Heart**

F. Dreyfuss, M. Ben-Porath, and J. Menczel. *American Journal of Cardiology* [*Amer. J. Cardiol.*] **6**, 237–245, Aug., 1960. 3 figs., 4 refs.

In a previous paper the authors demonstrated that a significantly higher isotope count was recorded over the praecordium than over the corresponding area of the right side of the chest in patients who had suffered a recent myocardial infarction (*Israel med. J.*, 1958, **17**, 219). In this paper they compare the radioactive iodine (^{131}I) uptake of the heart in 23 patients with myocardial infarction and 21 control subjects who were seen at Rothschild-Hadassah University Hospital, Jerusalem. The patients were given 100 μc. of ^{131}I and isotope counts were recorded daily at the electrocardiographic location of Leads V3 and V5 on both sides of the chest by means of a directional scintillation counter, starting 24 hours after the administration of ^{131}I and being continued daily for up to 2 weeks. The results were expressed as the left-to-right (L:R) ratio, that is, the difference in the counts over corresponding points of the two sides of the chest after deduction of the body background counts which were obtained over the calves. If a point on the chest wall overlying the heart was found to have a higher count than that at V3 or V5, this reading was recorded

and compared with the count at the corresponding contralateral point.

It was found that all patients with myocardial infarction showed an increased uptake of ^{131}I over the infarcted area as compared with that at the corresponding point on the right chest. Such increased L:R ratios were mostly found either 1 to 2 or 6 to 7 days after the administration of ^{131}I. To a certain extent the location of the increased L:R ratio made it possible to determine whether the infarct was anterior or posterior. One patient, who had been given ^{131}I 3 days after the acute infarction, died on the seventh day; examination of the heart on the following day showed increased counts (600 per minute per g.) over the 2 posterior infarcts, compared with 300 to 400 over other parts of the heart. In most of the control subjects the L:R ratio was about one; they did not show any constant elevation of counts over the heart, and although an occasional L:R ratio of 1·2 (borderline) or more was observed these subjects were clearly distinguishable from the patients with infarction. It appears that damaged heart muscle or its immediate surroundings accumulate ^{131}I, but the underlying mechanism of this as well as the frequently found dip in the L:R ratio on the third day are still unexplained.

A. Schott

486. **Electrocardiographic Evaluation of Pulmonic Stenosis**

M. A. Engle, T. Ito, D. S. Lukas, and H. P. Goldberg. *Journal of Pediatrics* [*J. Pediat.*] **57**, 171–179, Aug., 1960. 6 figs., 18 refs.

An analysis is presented of the electrocardiograms (ECG) obtained close to the time of cardiac catheterization in 73 patients with pure pulmonary stenosis admitted to the New York Hospital. It was found that the ECG gave an accurate impression of the burden on the right ventricle both pre- and post-operatively. When the tracing was normal right ventricular systolic pressure was below 50 mm. Hg and when it showed only right axis deviation, or a predominant R wave of less than 10 mm., or an rsr pattern in Lead V1 the pressure was under 80 mm. Hg. Abnormalities of P waves and T waves or ST segments were not observed at this stage. In cases where the R wave in Lead V1 was more than 10 mm. in amplitude, the pressure was over 80 mm. Hg and when the S wave was the predominant deflection in Leads V5 or V6 the pressure was 100 mm. Hg or more. If the right ventricular systolic pressure was over 140 mm. Hg the R wave in Lead V1 exceeded 20 mm. and other abnormalities appeared, such as peaked P waves, leftward displacement of the transitional zone, and deep inversion of T waves in the right precordial leads. Above 140 mm. Hg these abnormalities were exaggerated and half the tracings showed a qR configuration in the right precordial leads.

The height of the R wave in Lead V1 was the best guide, but no single ECG sign was reliable in all patients. With the composite ECG evaluation described it is possible to distinguish patients with mild, moderate, or severe stenosis and to assess improvement after operation.

T. Semple

487. **Specificity of the Current Electrocardiographic Criteria in the Diagnosis of Left Ventricular Hypertrophy**

Te-Chuan Chou, R. C. Scott, R. W. Booth, and H. B. McWhorter. *American Heart Journal* [*Amer. Heart J.*] **60**, 371–377, Sept., 1960. 9 refs.

An analysis of the autopsy findings in 100 cases of left ventricular hypertrophy (L.V.H.), diagnosed by the electrocardiogram, revealed 44 cases of isolated L.V.H., 45 cases of combined left and right ventricular hypertrophy (C.V.H.), one case of isolated right ventricular hypertrophy (R.V.H.), one case of no ventricular hypertrophy, and 9 cases of questionable hypertrophy. High voltage in the precordial leads was the most useful but least specific criterion for L.V.H. The presence of increased voltage in the limb leads or other signs in addition to the high voltage increased the specificity. Differentiation of C.V.H. from isolated L.V.H. by the electrocardiogram was rarely possible by the currently available methods.

The presence of anatomic L.V.H. made some of the electrocardiographic criteria for R.V.H. unreliable.—[Authors' summary.]

488. **The Electrocardiogram, Spatial Vectorcardiogram, and Ventricular Gradient in Congenital Ventricular Septal Defect**

G. E. Burch and N. DePasquale. *American Heart Journal* [*Amer. Heart J.*] **60**, 195–211, Aug., 1960. 10 figs., 31 refs.

The electrocardiographic (ECG) findings in 110 patients in whom ventricular septal defect was the only abnormality demonstrated by cardiac catheterization are described in this paper from the Charity Hospital of Louisiana, New Orleans. Three-quarters of the patients (77) were children under 10 years of age.

In general the commonest ECG findings were prominent S waves in Leads I, II, V5, and V6 and an R′ wave in Lead V1. This was interpreted, in conjunction with the vector cardiogram, as hypertrophy of the right ventricle in whole or in part (65% of the patients). There was little evidence of left ventricular hypertrophy, but the presence of a deep Q wave in Leads V5 and V6 (in 35%) may have been due to hypertrophy of the septal part of the left ventricle. Correlation of the ECG and catheterization findings showed that, in cases with higher right ventricular pressures, the R:S ratio tended to increase in Lead V1 and to decrease in Lead V6, and the A–QRS complex was oriented more to the right. The ventricular gradient was abnormal in direction or magnitude in half the cases, suggesting that this is a more sensitive index of abnormalities of myocardial activity than is T-wave change (seen in only 18%).

Spatial vectorcardiograms were studied in 25 cases, and a few of these are reproduced and analysed. The important suggestion is made that the ECG pattern of "partial right bundle-branch block" with S waves in Leads I and II, which is shown spatially as a late extension of the frontal QRS loop upwards and to the right, is caused by hypertrophy of the crista supraventricularis in the outflow part of the right ventricle. Anatomical proof that this is present is still awaited.

J. A. Cosh

489. **Ballistocardiographic Changes in Cardiac Infarction.** (Изменения баллистокардиограммы при инфарктах сердца)
I. M. Hejnonen and A. N. Kokosov. *Терапевтический Архив* [*Ter. Arh.*] **32**, 75–83, Aug., 1960. 3 figs., 7 refs.

The authors report that the electromagnetic monitor designed by Bayevskii makes it possible to obtain ballistocardiograms in patients with myocardial infarction without disturbing their rest. The technique employed combines the features of the direct method of Star and the indirect method of Dock. In this study 33 patients with a first infarction and 28 with 2nd or 3rd episodes were investigated by this means, 66 tracings in all being obtained. The changes most commonly observed were: 3 waves on one line, an earlier M wave, accentuated diastolic waves against the general background of subnormal cardiac output, a bifurcated I wave and a shortened K; the determination of numerical indices proved less significant.

Ballistocardiography is an important diagnostic procedure, especially if comparison with previous tracings is possible. In the presence of infarction such a comparison reveals the rapid and marked deterioration (Brown's scale), the appearance of signs of coronary insufficiency, and a relative increased or marked reduction of "maximum body velocity", with a ballistic index under 0·4. The changes are less obvious in subsequent infarcts, but they are accentuated by pre-existent hypertension. The chief prognostic value of ballistocardiography lies in the fact that, being more sensitive, it gives a better indication of the contractile power of the myocardium and the state of the coronary circulation than does the electrocardiogram. In the recovery period ballistocardiography also provides a better indication of the rate of improvement and the amount of physical exertion of which the patient is capable. A persistent 4th degree tracing is usually of bad prognostic significance. However, it is pointed out that in considering the prognosis preference must be given to the clinical evidence.

S. W. Waydenfeld

DISTURBANCES OF RHYTHM AND CONDUCTION

490. **Intravenous Use of Lidocaine for Ventricular Arrhythmias**
W. A. Weiss. *Anesthesia and Analgesia; Current Researches* [*Anesth. Analg. curr. Res.*] **39**, 369–381, July–Aug., 1960. 4 figs., 5 refs.

The author describes his experience in 148 patients of 2% lignocaine in the prevention and treatment of ventricular arrhythmias during closed cardiac operations. The drug was given in a dosage of 1 mg. per 2 or 3 lb. (1 mg. per 0·9 or 1·35 kg.) body weight. Conversion of ventricular arrhythmia was achieved in 126 of the patients. Lignocaine was also used prophylactically during transventricular aortic commissurotomy in 24 patients and it uniformly prevented the occurrence of alarming ventricular irregularities. Similar favourable results were obtained in patients undergoing open cardiac surgery under hypothermia. The results are briefly discussed and electrocardiographic tracings are reproduced.

Mark Swerdlow

491. **Disturbances of Conduction after Intracardiac Operations.** (Troubles des conduction consécutifs à la chirurgie intracardiaque)
M. Blondeau and J. Lenègre. *Archives des maladies du cœur et des vaisseaux* [*Arch. Mal. Cœur*] **53**, 740–756, July [received Sept.], **53**, 740–756, July [received Sept.], 1960. 5 figs., 10 refs.

One of the complications of intracardiac surgery, especially for the treatment of septal or para-septal defects, is the incidental damage caused to the conducting pathways of the heart. From the Hôpital Boucicaut, Paris, the authors describe their experience in 102 successive intracardiac operations (other than mitral commissurotomies) in which postoperative electrocardiograms (ECGs) were taken. Of this number 29 were closed-heart operations necessitating ventriculotomy on one or both sides, and 73 were open-heart operations, some performed under hypothermia and some with the aid of an extracorporeal circulation. In most cases the ECGs were recorded more than 15 hours after operation.

Of the 29 closed-heart operations in only 2 did bundle-branch block (B.B.B.) ensue, whereas 27 of the 73 open-heart operations were followed by conduction troubles. These cases are analysed according to the pre-existing lesions and the type of disturbances found. Thus there were 7 cases of atrio-ventricular (A–V) block, 17 of complete, 4 of incomplete right B.B.B., and one of complete left B.B.B. The over-all incidence of disturbances of conduction following intracardiac surgery reaches almost 30% in the type of case studied, but it is only 7% in closed-heart operations as against 37% if the heart is opened. In the latter group the tendency to conduction disturbances varies with the type of cardiac lesion: thus operation for a high or intermediately situated patent interauricular septum causes no such disturbances, and in only one case of pulmonary valvulotomy did they arise. In the repair of a low patent interauricular septum, however, or of the A–V canal the frequency is increased, while in operations for patent interventricular septum and infundibular pulmonary stenosis conduction troubles are almost certain to occur. The 7 cases of A–V block observed in this series followed the insertion of a prosthesis to close a low interauricular or a high interventricular septal defect, and in all 7 the disturbance of conduction was of grave significance. Histological examination of post-mortem material in these cases showed that the bundle of His and its bifurcation may be involved by suture material. In the case of partial or complete right B.B.B. the aetiological mechanism is not so clear. It does not appear to affect adversely the immediate or delayed postoperative prognosis.

R. Wyburn-Mason

492. **Atrial Tachycardia with Atrioventricular Block Due to Digitalis Poisoning**
E. A. Harris, D. G. Julian, and M. F. Oliver. *British Medical Journal* [*Brit. med. J.*] **2**, 1409–1413, Nov. 12, 1960. 3 figs., 7 refs.

CORONARY DISEASE AND MYOCARDIAL INFARCTION

493. **Diagnostic Value of C-Reactive Protein in Stenocardia and Acute Myocardial Infarction.** (К вопросу о диагностической ценности С-реактивного белка при стенокардии и остром инфаркте миокарда)
N. P. MASLOVA. *Терапевтический Архив* [*Ter. Arh.*] **32**, 62–65, Aug., 1960. 17 refs.

In this investigation, which was prompted by the difficulties encountered in the diagnosis of various forms of coronary insufficiency, the level of C-reactive protein was determined by precipitation by immune rabbit serum (this proving the simplest and most suitable of several methods tried) in the serum of 127 patients admitted to hospital with the preliminary diagnosis of acute myocardial infarction.

The test, which was carried out on the first and second day after admission when the clinical diagnosis was still doubtful, gave a negative result in 70 cases and a positive result in 57. Of the latter group confirmation of acute myocardial infarction was obtained clinically in 46, while 10 were found to be suffering from angina pectoris and pneumonia and one from angina and acute cholecystitis. No infarct could be demonstrated in any of 70 patients in whom the reaction was negative and a diagnosis of angina was made. The reaction was also negative in 15 healthy control subjects.

In the positive cases the quantitative reaction showed diminishing amounts of C-reactive protein, and finally its complete disappearance with clinical recovery towards the 18th to 20th day, though in a few cases not until the 30th to the 40th day. In 7 patients with micro-infarcts the initial amount of C-reactive protein was less and it had already disappeared by the 10th to the 15th day. The author states that failure of the C-reactive protein to disappear in time is of grave prognostic significance. She concludes that the reaction is of great value in the differentiation of stenocardia from acute myocardial infarction. *S. W. Waydenfeld*

494. **Electrokymographic Changes in Myocardial Infarction.** [In English]
O. BARTLEY. *Acta radiologica* [*Acta radiol. (Stockh.)*] **54**, 81–89, Aug., 1960. 5 figs., 12 refs.

An infarcted portion of the left ventricular wall may fail to take part in contraction during systole, and may even undergo paradoxical movement—that is, expansion. Such abnormal patterns of movement are well illustrated in this study from Sahlgrenska Sjukhuset, Gothenburg, Sweden. A direct-writing instrument was used, simultaneously recording the electrocardiogram and the heart sounds. Of 36 patients who had previously had cardiac infarction paradoxical movement was found in 7 and lesser abnormalities in a further 27. Studies of atrial movement showed a late contraction of the left atrium, resembling the change due to mitral stenosis, in 28 of the 35 patients in sinus rhythm. Minor changes in the movement pattern of the pulmonary artery were seen in 14 out of 35.

Such records need to be interpreted with some reserve as apparent paradoxical movement can be seen without infarction. To be reliable the recording must be made with held breath, and it must be shown that the abnormal movement is confined to one part of the ventricular wall. *J. A. Cosh*

495. **Prognosis of Angina Pectoris and Myocardial Infarction: Further Report**
L. H. SIGLER. *American Journal of Cardiology* [*Amer. J. Cardiol.*] **6**, 252–258, Aug., 1960. 8 refs.

This paper presents a follow-up study for an additional period of 9 years of 565 of the 1,700 patients with coronary arterial disease whom the author originally kept under observation for 25 years, as previously described (*J. Amer. med. Ass.*, 1951, **146**, 998; *Abstr. Wld Med.*, 1951, **10**, 510). At the end of this second period 217 men and 78 women had died and 227 men and 43 women were alive. Figures for the average periods of survival in these groups are given. In the "living group" the survival rates for men and women were as follows: at the end of 5 years 91·2 and 88·3% respectively; after 10 years 65·2 and 58·1%, and after 15 years 11 and 16·3% respectively. The mean age at death was 61·3 years for men and 66·9 for women. The mean time which the patients still alive had survived after the first attack of coronary occlusion was nearly 11 years, and in the patients who had died the mean survival period had been 8 years for men and 8·3 years for women. It is concluded that the prognosis of the disease is far better than has generally been reported. The detailed figures are given in tabular form. *A. Schott*

496. **Long Term Influence of the Beck Operation for Coronary Heart Disease**
B. L. BROFMAN. *American Journal of Cardiology* [*Amer. J. Cardiol.*] **6**, 259–271, Aug., 1960. 4 figs., 46 refs.

Since January, 1954, some 600 patients with coronary arterial disease have been subjected to surgery at Mount Sinai Hospital and the University Hospitals, Cleveland, Ohio, the technique employed being one evolved from the "Beck-II" operation and from various modifications of the Beck-I procedure for increasing the blood supply to the myocardium.

In this paper the author analyses the subsequent fate of 110 of these patients who were followed up for an average period of 4 years. Of these, 24 (22%) have since died, but the results were considered excellent in 43 (39%), these patients having little or no pain and being able to work full time. In a further 34 (30·8%) the response to operation was classified as good; these patients still had occasional symptoms on exertion or emotional stress, which, however, were readily controlled by trinitrin or rest, and all of them were able to do considerably more work than before the operation. Of the remainder, there was little apparent improvement in 7 patients, these being still limited in their activities by the recurrence of symptoms; some of them had had one or more moderately severe heart attack since the operation. In 2 cases (1·8%) there was no apparent benefit from surgery. The detailed case histories of 13 patients are presented to illustrate various aspects of the effect of the Beck operation. *A. Schott*

SYSTEMIC CIRCULATORY DISORDERS

497. **The Carotid-sinus Syndrome**
E. C. HUTCHINSON and J. P. P. STOCK. *Lancet* [*Lancet*] **2**, 445–449, Aug. 27, 1960. 2 figs., 16 refs.

The authors of this paper from the Stoke-on-Trent Hospital Group review 16 cases of the carotid-sinus syndrome seen over a period of 2 years. Most of the patients (males, aged 48 to 82 years) had some degree of hypertension. The right sinus was affected in 14 cases, and the left in 2. The main presenting symptoms in descending order of frequency were vertigo, syncope, focal attacks, and mental changes. In one patient permanent dementia with bilateral pyramidal involvement developed as a result of cerebral ischaemia during temporary cardiac standstill. In some of the cases Ménière's syndrome and idiopathic epilepsy had been mistakenly diagnosed.

Atropine controlled the milder manifestations, but in 8 cases the attacks were abolished by denervation of the affected sinus. Changes in arterial pressure recorded during induced attacks in 13 cases are shown in graphs and the pathogenesis of the syndrome is discussed. The problem of the so-called cerebral form of the syndrome, in which it is said symptoms can be induced by carotid-sinus stimulation without demonstrable circulatory changes, is discussed at length.

[A surgical note describing the technique of denervation of the sinus completes this very convincing and interesting report.] *A. J. Karlish*

498. **Circulatory Effects of Guanethidine. Clinical, Renal, and Cardiac Responses to Treatment with a Novel Antihypertensive Drug**
D. W. RICHARDSON, E. M. WYSO, J. H. MAGEE, and G. C. CAVELL. *Circulation* [*Circulation*] **22**, 184–190, Aug., 1960. 4 figs., 10 refs.

At the Veterans Administration Hospital, Richmond, Virginia, 25 male patients with severe hypertensive disease were treated with guanethidine for periods up to 6 months. A satisfactory reduction in blood pressure in the supine and standing positions was achieved in all cases, but 15 patients complained of orthostatic dizziness or fainting and several had mild diarrhoea. In 21 patients cardiac output was measured by a dye-dilution technique before treatment and again about one week after guanethidine administration started, when the effect of the drug was usually at its maximum. There was a fall in cardiac output after guanethidine therapy, corresponding to the fall in blood pressure and unaccompanied by a significant change in peripheral vascular resistance. These findings support the view that guanethidine lowers blood pressure by inhibition of sympathetic venoconstrictor mechanisms with resultant pooling of blood in the legs and reduction of venous return.

Renal circulation was studied by clearance techniques in 11 patients before and during effective guanethidine treatment. Administration of the drug was accompanied by a marked reduction in glomerular filtration rate and renal plasma flow in 7 of the 11 patients in both the recumbent and the upright positions. The filtration fraction also decreased, but calculated renal vascular resistance diminished only slightly, indicating that the changes in renal circulation were caused by the reduction in blood pressure. In about half the patients treated with guanethidine, the blood urea nitrogen value rose appreciably during treatment, but renal function was never so seriously impaired as to require cessation of treatment.
Bernard Isaacs

499. **Selective Inhibition of the Sympathetic Nervous System in Man with Bretylium Tosylate, a New Antihypertensive Agent**
E. D. FREIS, T. SUGIURA, and D. LIPTAK. *Circulation* [*Circulation*] **22**, 191–197, Aug., 1960. 3 figs., 8 refs.

Experimental and clinical experience with bretylium tosylate in hypertension is reported in this paper from Georgetown University School of Medicine, Washington, D.C. In normotensive subjects both the hypertensive " overshoot " which follows the Valsalva manœuvre and the digital vasoconstrictor response to a deep breath were partially inhibited by 50 mg. of bretylium tosylate intravenously and completely inhibited by 150 mg., while the cold pressor response was inhibited but not completely blocked by 150 mg. of the drug. In 4 hypertensive patients the ratio of effective oral to effective intravenous dosage was measured by the smallest dose required to produce orthostatic hypotension and found to vary from 8:1 to 24:1, indicating poor oral absorption of the drug.

Bretylium tosylate was administered either alone or in combination with chlorothiazide, or hydrochlorazide, or hydrallazine to 16 ambulant patients with moderately severe hypertension for periods varying from 1 to 5 months. Most patients required 1,800 to 2,400 mg. of bretylium tosylate daily without adjunctive therapy, or 1,000 to 1,200 mg. daily with adjunctive therapy, although some failed to respond even to 3,000 mg. daily. Orthostatic faintness, failure of ejaculation, and pain over the parotid glands were the only side-effects. Accurate adjustment of dosage to individual requirements was always necessary.

The authors consider that bretylium tosylate is of value in patients with severe disease whose hypertension cannot be controlled with chlorothiazide either alone or with small doses of hydrallazine or reserpine, but in cases remaining unresponsive to an acceptable dose of the drug recourse should be had to guanethidine or ganglion-blocking agents. *Bernard Isaacs*

500. **Bretylium Tosylate: Long-term Clinical Trial of New Hypotensive Agent**
D. STUCKEY. *Medical Journal of Australia* [*Med. J. Aust.*] **2**, 166–168, July 30, 1960. 11 refs.

The ability of bretylium tosylate to control hypertension for long periods of time was investigated at the Royal North Shore Hospital, Sydney, and the author here describes the response of an unselected series of 20 hypertensive patients who were treated for several months with this drug, together with chlorothiazide, reserpine, or hydrallazine. The criteria for his various diagnostic sub-divisions and the method used in recording

the blood pressure were detailed in a previous paper (*Med. J. Aust.*, 1959, **2**, 349). The patients studied included 2 who had suffered a previous cerebral vascular accident, 5 with attacks of left ventricular failure, 6 with evidence of renal failure, 3 with malignant hypertension, and 3 who were diagnosed as having hypertension of renal origin. The daily dose of chlorothiazide was 1 g. and that of reserpine 0·5 to 0·75 mg. The 3 cases receiving hydrallazine were given a daily dosage of 150 mg.

The initial response of the 20 patients was classified as excellent in 11, good in 5, fair in one, poor in one, and unsatisfactory in 2. The later assessment, however, was less promising, being excellent in only 2, good in 6, fair in 4, poor in one, and unsatisfactory in 7. Side-effects, which were severe enough in 4 instances to necessitate the withdrawal of the drug, consisted of vomiting (2 cases), diarrhoea (2), muscular pain (3), muscular weakness (3), headache (2), and dizziness which was not postural (4). Nasal congestion and parotid pain did not occur, but hypotensive attacks with syncope, which often came on without warning while walking in the street, was observed in 4 patients. The attacks were not precipitated when the patient stood up after being in the supine position, but they were relieved by lying down. Tolerance to the drug was noted in 10 of the 20 patients and prevented adequate control of the blood pressure in 4 of these. In 13 cases bretylium tosylate was discontinued either because increasing tolerance to its action made control impossible or (4 cases) because of side-effects (vomiting in one instance and profound muscular weakness in 3). However, in 7 patients the blood pressure was kept under adequate control with bretylium tosylate, although 3 of these were also receiving hydrallazine.

The author concludes that bretylium tosylate has a place in the long-term management of patients with moderately severe hypertension, provided they do not show any instability or a tendency to become tolerant to the drug. For this comparatively small group bretylium tosylate controls hypertension in a manner which is relatively pleasant when compared with other forms of treatment. *J. Warwick Buckler*

501. **Acquired Tolerance to Bretylium Tosylate ("Darenthin") in the Treatment of Hypertension**

R. L. Hodge and J. M. McPhie. *Medical Journal of Australia* [*Med. J. Aust.*] **2**, 169–172, July 30, 1960. 4 figs., 6 refs.

The development of tolerance to bretylium tosylate in hypertensive patients who are maintained on the drug for long periods presents a serious problem. In this paper from the Royal Adelaide Hospital, Australia, the authors report the effects of bretylium tosylate in 9 hypertensive patients who received the drug for 6 months. All of them had a diastolic blood pressure of at least 100 mm. Hg and a systolic pressure of at least 190 mm. Hg, associated with a Grade-II retinopathy, electrocardiographic evidence of left ventricular hypertrophy, or radiological evidence of left ventricular enlargement. Six of the 9 patients, who were aged 41 to 60 years, had previously received hypotensive therapy. All patients were given 0·5 g. of chlorothiazide daily throughout the trial, but all other therapy with the exception of digitalis was withdrawn. The initial dosage of bretylium tosylate was 100 mg. 3 times daily 30 minutes before meals. Subsequent increases in dosage, varying from 100 to 300 mg. daily, were administered when the patients became ambulant. During the period in hospital the blood pressure was recorded 2 hours after each dose of bretylium tosylate. Patients were discharged from hospital when the blood pressure was considered to be satisfactorily controlled; follow-up examination was carried out on at least one morning and one afternoon per week at the out-patient clinic.

Of the 9 patients only 2 were satisfactorily controlled on a constant dose of the drug, but 6 were controlled adequately if the dose of bretylium tosylate was steadily increased. In one case the hypertension could not be controlled even with a daily dosage of 3·6 g. Side-effects consisted in parotid pain in 2 patients, which in one was so severe that treatment had to be withdrawn. Nasal congestion occurred in all the patients at the start of therapy, but subsided later. In the opinion of the authors the development of tolerance in their cases constitutes the most serious practical objection to long-term therapy with bretylium tosylate, particularly in view of the high cost and the frequent medical supervision found necessary. They also found that it was not possible to predict, even in retrospect, those patients who would acquire drug tolerance and those in whom the blood pressure would remain stable on a particular dosage. *J. Warwick Buckler*

502. **The Course of Retinopathy in Treated Malignant Hypertension**

G. Lockhart, G. von Noorden, H. P. Dustan, A. C. Corcoran, and I. H. Page. *Archives of Internal Medicine* [*Arch. intern. Med.*] **106**, 205–212, Aug., 1960. 5 figs., 18 refs.

A study of the relationship between the severity of retinopathy and the progress of malignant hypertension is reported from the Department of Ophthalmology and the Research Division of the Cleveland Clinic Foundation, Ohio. Of a total of 96 patients 49 "failed to survive". At the first examination papilloedema and retinal exudates were more marked and the degree of heart disease more severe in the patients who died than in the survivors, but haemorrhages, arteriolar constriction and sclerosis, and renal damage were no more pronounced in this group than in the survivors. Papilloedema, haemorrhages, and retinal exudates disappeared in those patients in whom the blood pressure was well controlled; arteriolar sclerosis and constriction were unaffected. In the patients who died papilloedema and retinal exudates had persisted. *David Phear*

503. **A Further Case of the Budd–Chiari Syndrome.** (A propos d'un nouveau cas de syndrome de Budd-Chiari)

J. Catinat, J. Auvert, P. Casassus, C. Nezelof, and J. L. Roy. *Presse médicale* [*Presse méd.*] **68**, 1749–1752, Oct. 26, 1960. 10 figs., 5 refs.

Clinical Haematology

504. **Massive Nitrogen Mustard Therapy in Hodgkin's Disease with Protection of Bone Marrow by Tourniquets**
M. E. CONRAD JR. and W. H. CROSBY. *Blood* [*Blood*] **16**, 1089–1103, Aug., 1960. 6 figs., 16 refs.

Massive single doses of nitrogen mustard (0·95 to 1·5 mg. per kg. body weight) were given to 8 patients with previously treated advanced Hodgkin's disease at the Walter Reed General Hospital, Washington. In order to protect the bone marrow orthopaedic tourniquets at a pressure of 575 mm. Hg over the thighs and 375 mm. Hg over the arms were applied under anaesthesia for 15 minutes while the infusion was given. The leucocyte count reached its lowest value in 6 to 8 days and the platelet count between the 9th and 15th days. Increased activity of the protected marrow was seen when the marrow proximal to the tourniquets was aplastic. Tumour regression was observed in all cases, remissions lasting 41 to 240 days. Complications included vascular headache, tinnitus, deafness, alopecia, and thrombophlebitis. There was no evidence of significant gastrointestinal toxicity. The authors state that dividing the massive dose appeared to diminish toxicity. *I. Ansell*

505. **Studies on Thrombopoiesis. I. A Factor in Normal Human Plasma Required for Platelet Production; Chronic Thrombocytopenia Due to Its Deficiency**
I. SCHULMAN, M. PIERCE, A. LUKENS, and Z. CURRIMBHOY. *Blood* [*Blood*] **16**, 943–957, July, 1960. 9 figs., 16 refs.

A case of chronic thrombocytopenic purpura which appeared to be due to the congenital deficiency of a platelet-stimulating factor in the plasma is described.

An 8-year-old girl was admitted to the Children's Memorial Hospital, Chicago, suffering from thrombocytopenic purpura, which was only transiently improved by splenectomy and was unaffected by administration of steroids. Transfusion of whole blood was followed by a striking rise in the platelet count, an observation which prompted the studies reported in this paper. In a series of 45 investigations carried out over the past 5 years normal or increased platelet levels were observed after transfusion of fresh or stored whole blood, fresh or stored plasma, or fresh frozen plasma, maximum levels being reached 9 to 11 days after transfusion and baseline levels after 20 to 23 days. The platelet count rose to 280,000 per c.mm. following injection of as little as 1·9 ml. of fresh frozen plasma per kg. body weight and to 700,000 to 1,000,000 after injection of 7 ml. per kg. Serial marrow examinations indicated that the plasma factor stimulated megakaryocyte maturation and platelet formation, but that erythrocyte and leucocyte counts were unaffected. The presence of the spleen appeared partially to inhibit the platelet response, since much higher levels were obtained after splenectomy. During the thrombocytopenic periods there were episodes of icterus, one of which appeared to be due to hepatitis; no evidence of haemolysis was observed in the others, and their pathogenesis has not been elucidated. Plasma from the patient's father produced suboptimal platelet levels in the patient, but in both parents the platelet count was normal.

The authors consider that the thrombocytopenia was due to congenital deficiency of a factor which is present in normal plasma and is necessary for megakaryocyte maturation and platelet production. The relationship of this factor to erythropoietin is discussed.

J. L. Markson

506. **Hemoglobin H Associated with an Uncommon Variant of Thalassemia Trait**
W. A. DITTMAN, A. HAUT, M. M. WINTROBE, and G. E. CARTWRIGHT. *Blood* [*Blood*] **16**, 975–983, July, 1960. 6 figs., 28 refs.

Most abnormal haemoglobins show evidence of familial transmission. A 26-year-old American woman of Sardinian extraction was admitted to Salt Lake County General Hospital, Utah, with hypochromic anaemia, a normal serum iron level, and a history of chronic haemolytic anaemia. Detailed investigations indicated that this was a case of haemoglobin H–thalassaemia disease, but, in contrast to typical uncomplicated thalassaemia minor, in which increased amounts of A_2 haemoglobin are found, the A_2 component in this case was reduced. The patient's mother, sister, and son all showed haematological features of the thalassaemia trait, but no increase in A_2 values. The occurrence of haemoglobin H has been reported only in conjunction with the " thalassaemia trait ", but A_2 values in near relatives have been reported in only one other study apart from the present one. The significance of these observations can only be determined when more information is available on A_2 values in " thalassaemia trait " relatives in other haemoglobin-H pedigrees.

J. L. Markson

507. **Neutralization of Heparin by Means of Protamine after Operations Performed with Extracorporeal Circulation.** (La neutralisation de l'héparine par la protamine au décours des interventions sous circulation extracorporelle)
G. DUBOURG, M. TRARIEUX, F. FONTAN, J. MOULINIER, H. BRICAUD, and P. BROUSTET. *Revue française d'études cliniques et biologiques* [*Rev. franç. Ét. clin. biol.*] **5**, 691–696, Aug.–Sept., 1960. 9 refs.

Writing from the Hôpital du Tondu, Bordeaux, the authors stress the importance of adequate neutralization of heparin after the use of extracorporeal circulation for major heart surgery, their recent experience being based on 40 operations for congenital heart disease. Preoperative coagulation studies were performed in all cases and 2 mg. of heparin per kg. body weight was given for

the operation. On disconnecting the catheters the first "test" dose of protamine was given and 30 minutes later the clotting time (Lee–White) was determined and a thrombelastogram, to run over 4 hours, started. If the clotting time was less than 30 minutes, the thrombelastogram constant (r) less than 20 minutes, and the r+k constant less than 30 minutes no further protamine was given. Otherwise a further dose of protamine was given (one hour later in 25 cases and 2 hours later in 4) and the tests repeated. [The "test" dose of protamine is said to equal the amount of heparin in mg., expressed as 100%, but from the authors' table it appears that in all cases in which a second dose of protamine was necessary, the maximum test dose amounted to only 50% of the dose of heparin.]

Of the 37 cases finally summarized, 14 evolved towards hypercoagulability, 18 towards isocoagulability, and 5 towards hypocoagulability (which, however, became normal later). Preoperative coagulation defects did not affect the postoperative state. It did not appear to matter whether protamine was given by continuous or fractionated injection. The dose of protamine varied between 50 and 100% of that of heparin. The results, presented in a table, show that there is no predictable correlation between protamine dosage and final blood coagulability, except that all patients who received protamine over the 100% level (that is, greater than the dose of heparin) tended towards hypercoagulability, although the latter occasionally occurred with a protamine dose as low as 50%.

The authors prefer thrombelastography to other methods of determining clotting time, because it allows platelet function and fibrinogen content also to be estimated. They consider that the reported figure, based on studies *in vitro*, of 100 mg. of protamine for every 150 mg. of heparin is not applicable to studies *in vivo*. Some of the thrombelastograms obtained in this study suggested the development of thrombocytopenia (occasionally confirmed) and they are therefore inclined to increase the dose of heparin. The one death occurring in the series was due to an uncontrollable haemorrhage; in this case the thrombelastogram suggested that there was afibrinogenaemia, which could have been due to a fibrinolysin or a circulating anticoagulant.

F. Hillman

508. **Congenital Vascular Defect Associated with Platelet Abnormality and Antihemophilic Factor Deficiency**

G. Raccuglia and J. V. Neel. *Blood* [*Blood*] **15**, 807–829, June, 1960. 4 figs., bibliography.

At the University of Michigan Medical School, Ann Arbor, the authors studied 311 members of a large kindred many of whom exhibited a bleeding tendency. The manifestations varied greatly, the most frequent being oral bleeding, ecchymoses and haematomata, excessive bleeding after trauma, vaginal haemorrhage, and epistaxis in that order. Three abnormalities—prolonged bleeding time, abnormality of platelets, and a plasma defect were variously combined. Most frequently the thrombin generation test and estimation of the bleeding time and the "silicone" clotting time gave abnormal results. The plasma was responsible for the defective thromboplastin generation since serum gave normal results. By direct estimation, the plasma abnormality was shown to be deficiency of the antihaemophilic factor (AHF) and confirmation was obtained by mixing experiments in which haemophilic blood was used. Prothrombin, Factor V, stable factors, and fibrinogen were within normal limits. Numerically, the platelets were seldom abnormal, but morphological abnormalities occurred especially in those cases in which depression of AHF and a prolonged bleeding time were observed. On the other hand, in one patient with a consistent plasma defect the bleeding time was always within normal limits. No explanation was found for the association between morphological platelet abnormalities and deficiency of AHF.

On the basis of probability the authors incline to the view that the defects are caused by a single dominant gene of variable expression. Sex linkage cannot be excluded. The present confused terminology of the congenital haemorrhagic diseases characterized by a prolonged bleeding time is emphasized. It is suggested that all such conditions should be described under the term "congenital vascular defect". *D. G. Adamson*

509. **A Comparative Study of Sterility Test Media in the Transfusion Service**

Z. Ježková. *Applied Microbiology* [*Appl. Microbiol.*] **8**, 274–277, Sept., 1960. 1 fig., 7 refs.

The importance of the detection of bacterial contamination in biological preparations (particularly blood derivatives) is the subject of this communication from the Institute of Haematology and Blood Transfusion, Prague. The author compared the sensitivity of Clausen's modified hydrosulphite medium, thioglycollate medium prepared according to the *U.S.P.* (1955), Bonnel's hydrosulphite medium, Brewer–Linden thioglycollate medium, and liver broth. Sets of these media were inoculated with one drop of a 24-hour culture of 272 strains of organisms, and to one half of the sets 0·5 ml. of plasma was added. Parallel incubation of these sets at 37°, 32°, and 22° C. was carried out.

The "cultivation capacity" was then graded from which it was seen that Clausen's and the *U.S.P.* thioglycollate media were superior to liver broth, Bonnel's medium, and the Brewer–Linden thioglycollate medium, in that order.

The author illustrates the results which she has obtained in a graph and gives a table showing details of the various bacteria which failed to grow in the different media. Representatives of 6 species failed to grow in Brewer–Linden broth, whereas only one species, *Flavobacterium*, failed once to grow in the *U.S.P.* XV medium. In general, the tubes which contained plasma showed a poorer growth than the plasma-free media. This finding is ascribed either to the bactericidal action of blood products or to autolysis.

The paper concludes with a brief outline of the sterility testing procedure employed in the Czechoslovak National Blood Transfusion Service, which records incidence of pyrexial reactions of 0·4%. *F. Hillman*

Respiratory System

510. **Treatment of Pneumococcal Pneumonia with a New Penicillin: Clinical Observations in 25 Patients**
P. A. BUNN and R. KNIGHT. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **240**, 192–196, Aug., 1960. 3 refs.

The response to potassium *alpha* phenoxyethyl penicillin (phenethicillin) of 25 patients with pneumococcal pneumonia is described in this paper from the State University of New York Upstate Medical School, Syracuse, New York. The first 15 patients received 500 mg. of the drug 6-hourly and the rest 250 mg. 3 times a day between meals. Serum concentrations were above 0·05 μg. per ml. for at least 4 hours after each dose and the results of treatment were good in both treatment groups. No untoward reactions and no complications were observed, and there were no deaths in the series. *I. Ansell*

511. **A Clinical Study of the Chronic Lung Disease Due to Nonphotochromogenic Acid-fast Bacilli**
A. G. LEWIS JR., E. M. LASCHÉ, A. L. ARMSTRONG, and F. P. DUNBAR. *Annals of Internal Medicine* [*Ann. intern. Med.*] **53**, 273–285, Aug. [received Oct.], 1960. 4 figs., 19 refs.

The authors describe 116 cases of chronic pulmonary disease due to atypical mycobacteria. Non-photochromogenic, acid-fast bacilli were isolated from these patients, who were receiving hospital treatment in Tampa, Florida.

The clinical features, which were indistinguishable from those of pulmonary tuberculosis, consisted in loss of weight, cough, haemoptysis, together with low grade pyrexia. Cavitation, pulmonary effusions, and calcification were seen on the radiographs. In general the x-ray appearances closely resembled those of pulmonary tuberculosis, except that the incidence of cavitation (78%) was significantly greater. The pulmonary disease, which was often associated with other diseases, showed a particularly high incidence in white males over the age of 40 years. Tuberculin skin testing with purified protein derivative (P.P.D.) and purified protein derivative made from purified non-photochromogen antigen (P.P.D.-B) was performed in 50 cases and also in 50 cases of proven tuberculosis. There was generally a reaction to both antigens, but almost invariably the homologous antigen produced a greater reaction. Bacteriologically the organism was differentiated from the tubercle bacillus by culture and by demonstrating its non-pathogenicity for guinea-pigs. Susceptibility studies showed that it was resistant to isoniazid and PAS, but displayed some sensitivity to streptomycin, cycloserine, viomycin, kanamycin, and sulphafurazole.

The results of treatment were disappointing. Of 78 patients treated medically 52·7% showed no radiological improvement on discharge. Cavity closure without surgery occurred in only 2 cases. The sputum remained positive for the organism in 43% of those treated medically. The over-all results of surgery were superior to those obtained with medical treatment. Pulmonary resection was performed on 37 patients and resulted in sputum conversion in 87% of this group. As many as 15 of the 17 patients who died received medical treatment only. There were 11 deaths from progressive lung disease associated with a superimposed bronchopneumonia or right heart failure and 3 from bronchial carcinoma. In 4 the primary lung disease was complicated by the development of pulmonary tuberculosis. The authors suggest the following four-point therapeutic regimen for these cases: (1) isolation from patients with pulmonary tuberculosis; (2) early recourse to thoracic surgery; (3) prophylactic administration of isoniazid together with two additional drugs to which the organism has been shown to be sensitive; and (4) discharge from hospital as soon as possible to avoid superinfection with drug-resistant tubercle bacilli. *J. Warwick Buckler*

512. **Observations on 100 Cases of Bronchial Carcinoma in a Rural Area**
B. R. HILLIS and J. A. CAMERON. *Thorax* [*Thorax*] **15**, 240–243, Sept., 1960. 25 refs.

One hundred cases of bronchial carcinoma arising in a rural area were examined for any significant differences in the disease as described in towns. Even though this is a non-industrial area [Dumfries and Galloway], and atmospheric pollution is extremely low, no outstanding difference was found. The relationship between smoking and bronchial carcinoma seems to hold in the country as in the town.—[Authors' summary.]

513. **Neurogenic Tumours of the Mediastinum: a Clinicopathologic Study**
L. S. CAREY, F. H. ELLIS JR., C. A. GOOD, and L. B. WOOLNER. *American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine* [*Amer. J. Roentgenol.*] **84**, 189–205, Aug., 1960. 9 figs., 6 refs.

The records of 140 patients with extrapleural mediastinal tumours of neurogenic origin treated surgically at the Mayo Clinic between 1923 and 1955 are reviewed. The clinicopathological features and the possibility of radiological diagnosis of various tumour types are discussed. A detailed follow-up analysis is included together with general considerations of the problem.
G. Calcutt

514. **Interstitial Pulmonary Fibrosis Secondary to Pulmonary Venous Hypertension: Report of a Case Due to Myxoma of the Left Atrium**
M. SOLOMON. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **174**, 464–467, Oct. 1, 1960. 3 figs., 8 refs.

Urogenital System

515. **Studies on Human Proteinuria. I. The Mechanism of Postural Proteinuria**
R. J. Slater, N. J. O'Doherty, and M. S. DeWolfe. *Pediatrics* [*Pediatrics*] **26**, 190–199, Aug., 1960. 17 refs.

The mechanism of postural proteinuria is still uncertain. It has been variously suggested (1) that the protein has passed the glomerular filter in large amounts, (2) that it is the allegedly normal filtered protein which has not been reabsorbed, or (3) that the protein is derived from lymph which is excreted into the renal pelvis.

At the Hospital for Sick Children, Toronto, the authors studied postural proteinuria in 5 children by injecting azovan blue to label the plasma albumin or injecting human serum albumin labelled with radioactive iodine (^{131}I). They found that the labelled albumin appeared in the urine very rapidly. If the dye was injected only after a period of lordosis, when recumbency was resumed, no dye appeared in the urine during the subsequent period of decreasing proteinuria. In the ^{131}I studies the specific radioactivities of the urinary and serum albumins were identical at a time when the radioactivity of the albumin of renal lymph would not be expected to be in equilibrium with that of plasma albumin. The electrophoretic pattern of the protein from urine and from serum was similar. The γ globulins in the urine were found to be similar to those of serum according to quantitative precipitin techniques, in contrast to the γ globulin excreted in exercise proteinuria and so-called normal proteinuria.

These findings suggest that the protein found in the urine due to postural changes has passed through the glomerular filter. *T. B. Begg*

516. **Recurrent Focal Nephritis**
J. H. Ross. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **29**, 391–406, July [received Sept.], 1960. 25 refs.

The author describes the clinical features of non-suppurative recurrent focal nephritis as seen in 9 patients treated at the London Hospital between 1945 and 1960. These patients, 7 male and 2 female, were aged between 6 and 25 years at onset of the disorder, which had persisted for varying periods up to 31 years; in 5 cases the first episode of frank haematuria occurred before the age of 10 years. The frequency and duration of the episodes of haematuria, which were sometimes accompanied by headache, pain in the neck and loin, and frequency and a burning sensation on micturition, were very variable. Respiratory symptoms and pyrexial attacks, during which the temperature rarely rose above 100° F. (37·8° C.) occurred in most cases before the onset of haematuria. All but one of the patients were examined in hospital during or shortly after bouts of haematuria, when hypertension and oedema were found to be virtually absent. One patient had a bullous skin eruption and angioneurotic oedema 10 days after the onset of the haematuria, while splenomegaly was observed in 4 cases. The erythrocyte sedimentation rate was usually normal, but slight anaemia was common. Persistent proteinuria, with an excess of erythrocytes and occasional granular and cellular casts in the urine, was the rule between the attacks. In 2 patients mild hypertension subsequently developed, but proved to be transient in one of them. The blood urea level was temporarily raised in 3 cases. Treatment with penicillin and by tonsillectomy did not influence the course of the disease and in 2 patients prednisone did not control the haematuria. Renal biopsy examination in 5 cases revealed focal glomerular lesions and slight focal increase in interstitial tissue in 3. The glomeruli showed local hypercellularity with adhesion to Bowman's capsule and sometimes slight local thickening of the basement membrane. One patient had more marked lesions, with focal perivascular and periglomerular fibrosis, while another had considerable increase in the interstitial tissue, with focal inflammatory cells and slight tubular atrophy.

The author considers that recurrent focal nephritis can be distinguished from acute diffuse nephritis (Ellis's Type I) and rapidly progressive Type-I nephritis by the absence of hypertension, oedema, and uraemia. He concludes that haemolytic streptococci are not important in its aetiology and that the course of the disease is benign in spite of the recurrent haematuria.
G. L. Asherson

517. **Hormone Therapy of the Adult Nephrotic Syndrome of Unknown Etiology**
R. S. Post and R. E. Eckel. *Journal of Chronic Diseases* [*J. chron. Dis.*] **12**, 211–242, Aug., 1960. 7 figs., 22 refs.

Corticotrophin and cortisone have a definite place in the treatment of the nephrotic syndrome in children, but their value in adults suffering from this condition is less well established. In this paper from Western Reserve University School of Medicine, Cleveland, Ohio, the authors describe the results obtained in 13 adults with a nephrotic syndrome of unknown aetiology, who were given one or more short courses of corticotrophin (20 to 40 mg. per day) intravenously or of prednisone (40 to 80 mg. per day) by mouth. There was a good response in 5 patients and, after repeated short courses of maximum tolerated doses, in 2 others, though 4 of them subsequently relapsed. These 4 patients were then given maintenance therapy consisting of intramuscular injections of corticotrophin 3 times a week, but there was a relapse when the drug was withdrawn. However, after further injections of corticotrophin 2 of the 4 had remissions lasting 8 months and 3½ years respectively, without treatment. In 6 patients there was no response to steroid therapy.

It is concluded that " adrenal cortical steroid hormones exert a beneficial effect on some adult patients " with an idiopathic nephrotic syndrome and that continued intermittent maintenance therapy will usually be required in these cases. *T. B. Begg*

Endocrinology

518. **Calcium Deprivation in Hypoparathyroidism: a Method of Diagnosis Using Sodium Phytate**
J. W. G. SMITH, R. H. DAVIS, and P. FOURMAN. *Lancet* [*Lancet*] **2**, 510–513, Sept. 3, 1960. 4 figs., 16 refs.

The existence of a state of parathyroid insufficiency in patients who have been subjected to thyroidectomy has been postulated. The ability of 14 such patients to withstand calcium deprivation was investigated at the Royal Infirmary, Cardiff, where they were given a diet low in calcium and sodium phytate. It was found that in those with clinical and biochemical hypoparathyroidism there was a sharp fall in plasma calcium levels and they developed tetany in 1 to 3 days. Further, 8 of them showed some evidence of hypoparathyroidism, as evidenced by a failure to maintain plasma calcium levels on the restricted calcium intake. The authors suggest that some degree of hypoparathyroidism is common after thyroidectomy and that this may often be misdiagnosed as an anxiety state, or even remain unrecognized. *I. McLean Baird*

THYROID GLAND

519. **The Evaluation of I^{131} Therapy of Graves' Disease: Reliability and Prognostic Value of Chemical and Radioactive Iodine Studies**
J. DOMNITZ, H. F. HURD, and J. W. GOLDZIEHER. *Archives of Internal Medicine* [*Arch. intern. Med.*] **106**, 194–204, Aug., 1960. 12 refs.

The results of radioactive-iodine (^{131}I) studies are reliable before treatment in patients with thyroid disease but after treatment they may be misleading. In this paper from Brooke General Hospital, Fort Sam Houston, Texas, the authors describe a study of thyroid function after ^{131}I treatment in 74 patients with diffuse toxic goitre, the uptake of the isotope by the thyroid gland at 6, 24, and 48 hours, the protein-bound ^{131}I conversion ratio, and the serum protein-bound iodine concentration measured chemically at 48 hours being correlated with the clinical assessment.

The results of the various thyroid function studies failed to agree with clinical assessment in from 10 to 60% of patients during the first year after treatment, but agreement was much closer after 12 months. During the first year the most reliable values were the uptake at 24 hours and at 48 hours, although they erred on the low side; with the other tests high values were obtained too often.

Patients who were clinically euthyroid remained so even if the laboratory tests revealed thyrotoxic values. The results of ^{131}I studies were in closest agreement with the clinical assessment in patients with persistent thyrotoxicosis, who usually need further treatment. Patients who remained clinically toxic but in whom the results of thyroid function studies were normal became euthyroid, but where both clinical and laboratory evidence indicated hypothyroidism this condition persisted in 50% of cases.

^{131}I studies after treatment showed a rapid turnover in the thyroid. In the authors' view this cannot be satisfactorily explained on the basis of "a reduced thyroidal iodine space with normal amounts of iodine handled by the gland", since the chemically estimated protein-bound iodine concentration was also high. They suggest that a protein-bound iodine fraction of reduced potency may be liberated, often in increased amounts, after ^{131}I treatment. *David Phear*

520. **Nodular Goiter. Incidence, Morphology before and after Iodine Prophylaxis, and Clinical Diagnosis**
R. P. STOFFER, J. W. WELCH, C. A. HELLWIG, V. E. CHESKY, and E. N. MCCUSKER. *Archives of Internal Medicine* [*Arch. intern. Med.*] **106**, 10–14, July, 1960. 17 refs.

This discussion of the incidence, morphology, and treatment of nodular goitre is based on a study of the records of 3,207 patients who were treated at the Hertzler Clinic, Halstead, Kansas, by surgery. In this series there were 206 (6·8%) with cancer of the thyroid, and it is noted that the incidence of malignancy increased after 1950, when iodized table salt was introduced in Kansas. There was also a marked increase in the number of colloid adenomata, but a decrease in the number of foetal adenomata. These structural changes in the features of nodular goitre have been reported from other countries where iodized salt is in general use.

The annual death rate from cancer of the thyroid in Kansas has nearly doubled since 1950, rising from a mean of 8 in the period 1940–9 to a mean of 13 in the period 1950–8. It was not possible to diagnose malignancy preoperatively in more than 31% of the undifferentiated and 9·3% of the well-differentiated cancers; studies of iodine uptake were of no assistance in the preoperative diagnosis of malignancy. In the authors' opinion thyroid extract or iodine are valueless in the treatment of nodular goitre and surgical removal is the treatment of choice, while at the same time every effort should be directed towards an earlier diagnosis.
J. Warwick Buckler

521. **New Aspects of Thyroid Therapy**
H. ZONDEK, H. E. LESZYNSKY, and G. W. ZONDEK. *Archives of Internal Medicine* [*Arch. intern. Med.*] **106**, 15–21, July, 1960. 6 refs.

The new aspect of thyroid therapy here described is an application of the so-called "stosstherapy" to three forms of inborn thyroid deficiency, and in this paper from Jerusalem the authors report the results obtained in 7 such patients by the administration of large doses of

triiodothyroacetic acid (triac) and of desiccated thyroid for short periods of 6 to 10 days.

A total treatment period of 2½ weeks per year produced remission of symptoms for 6 months in 2 cretinous siblings. A third sibling remained symptom-free for 6 months after treatment had ceased. The authors postulate that this form of treatment " acts in the manner of a trigger-mechanism through which the disordered interaction between specific thyroid enzymes and those cell particles responsible for hormone synthesis is restored, either by activation or by production of enzymatic agents ". In the other 4 patients, of whom 2 had primary myxoedema and 2 pituitary myxoedema, the treatment was ineffective. In the opinion of the authors, therefore, this treatment can produce long periods of remission without thyroid therapy, but only in those states of thyroid deficiency caused by intracellular functional defects in cell–enzyme relationship. They admit that such cases are rare compared with those of other thyroid deficiency states. *J. Warwick Buckler*

522. **Thyroglobulin Antibodies in Patients without Clinical Disease of the Thyroid Gland**
E. HACKETT, M. BEECH, and I. J. FORBES. *Lancet* [*Lancet*] **2**, 402–404, Aug. 20, 1960. 2 figs., 9 refs.

Some workers have reported that autoantibodies reacting *in vitro* with thyroglobulin can be isolated from the serum of patients with thyroid disease. The authors of this paper from the Department of Medicine, University of Adelaide, state that, using the tanned-cell haemagglutination technique, they found thyroid autoantibodies in the sera of 18% of 387 patients who had no clinical signs of thyroid disease, and in 42 (61%) of 69 with thyroid disease. Although there was no significant difference in the titre of autoantibodies in the two groups, all but one of the non-thyroid patients with titres of 1:5,120 and above were females, the youngest being 35 years (average age 56 years).

The authors suggest that the role of thyroglobulin antibodies found in the serum of patients without clinical evidence of thyroid disease is physiological rather than pathological. *D. G. Adamson*

ADRENAL GLANDS

523. **A Possible Explanation for Cushing's Syndrome Associated with Adrenal Hyperplasia**
C. A. NUGENT, K. EIK-NES, H. S. KENT, L. T. SAMUELS, and F. H. TYLER. *Journal of Clinical Endocrinology and Metabolism* [*J. clin. Endocr.*] **20**, 1259–1268, Sept., 1960. 5 figs., 17 refs.

Cushing's syndrome associated with bilateral adrenal hyperplasia can be satisfactorily explained by supposing that it results from an increased secretion of adrenocorticotrophic hormone (ACTH). However, it has not been possible to demonstrate a measurable increase in blood concentration of ACTH in such patients, and it has therefore been doubted that this is the explanation of the syndrome. In an investigation at the University of Utah College of Medicine, Salt Lake City, the effect on the plasma 17-hydroxycorticosteroid level of infusing amounts of ACTH insufficient to produce a measurable rise in the plasma levels of the hormone was determined in 7 normal young men. The amount of ACTH to be infused in each individual was determined by measuring the maximum quantity which could be infused intravenously for the 4 hours from 8 a.m. to noon without causing a rise in the plasma 17-hydroxycorticosteroid concentration. This was found to range from 1·5 to 5 i.u. per day. The appropriate concentration of ACTH was then infused constantly for 4 days. In 2 of the subjects 1 mg. of dexamethasone was given orally every 8 hours to suppress endogenous ACTH. In 4 of the 7 subjects, and including the 2 given dexamethasone, the plasma 17-hydroxycorticosteroid level was raised during the 4-day infusion. In 5 of the subjects the response of the plasma 17-hydroxycorticosteroid level to maximal stimulation with ACTH 2 hours after completion of the 4-day infusion was greater than it was when the same test was made before the infusion. It is concluded that the absence of a measurable increase in blood ACTH concentration in Cushing's syndrome associated with adrenal hyperplasia is not a valid objection to the hypothesis that the condition is due to a constant secretion of ACTH. *P. A. Nasmyth*

524. **Adrenocortical Function after Long-term Corticoid Therapy**
G. G. CARREON, J. J. CANARY, R. J. MEYER, and L. H. KYLE. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **56**, 235–244, Aug., 1960. 6 figs., 24 refs.

Prolonged suppression of adrenocortical function is observed after cessation of long-term glucocorticoid therapy. The reactivation achieved by administration of adrenocorticotrophic hormone (ACTH) may not be maintained when treatment is discontinued. In this paper from Georgetown University School of Medicine and Georgetown University Hospital, Washington, D.C., a study is reported of the urinary excretion of 17-ketosteroids and 17-hydroxysteroids in 3 patients who had received long-term glucocorticoid therapy. The first patient had had rheumatoid arthritis for 22 years and had been receiving 50 to 75 mg. of cortisone daily for the preceding 7 years. Liver and kidney function were normal, but for 3 days following the abrupt withdrawal of corticoid therapy steroid excretion was below normal. A standard 8-hour infusion of ACTH at the end of this short withdrawal period produced an increase in the excretion of 17-ketosteroids and 17-hydroxysteroids, but the response was subnormal. Sustained stimulation with intramuscular ACTH gel resulted in a urinary excretion of 17-hydroxysteroids which was above the normal level, but excretion of 17-ketosteroids, although increased, barely reached normal levels. When stimulation was discontinued the output of steroids fell below normal and 11 days after sustained stimulation there was a subnormal response to the standard ACTH test. A similar study was carried out in 2 other patients who had been receiving cortisone for 2½ and 3 years, respectively. The results were almost identical with those obtained in

the first patient, but in these last 2 patients a longer time was allowed to elapse between withdrawing corticoid therapy and beginning sustained stimulation with intramuscular ACTH gel. The maximum time between withdrawal and sustained stimulation was 7 days and during this time there was no evidence of a spontaneous return to normal excretion of 17-hydroxysteroids or 17-ketosteroids. Only one of the 3 patients gave an adequate response to the 8-hour ACTH test 10 days after stopping sustained stimulation with intramuscular ACTH gel.

P. A. Nasmyth

DIABETES MELLITUS

525. **Detection of Prediabetes by Glucose-tolerance test Sensitised by Prednisolone**

Y. GOTO, J. KATO, A. TAKANAMI, and A. OHNEDA. *Lancet* [*Lancet*] **2**, 461–465, Aug. 27, 1960. 4 figs., 19 refs.

The investigation described in this paper from Tohoku University Medical Faculty, Sendai, Japan, was undertaken to determine whether the pre-diabetic state can be demonstrated by the response to the glucose tolerance test sensitized with prednisolone, this test being carried out in 20 patients with diabetes mellitus, 17 healthy subjects with a family history of diabetes, 3 patients with a recent history of undetermined transient glycosuria, 9 patients with pancreatic disease of varying aetiology, 14 patients with diseases other than diabetes, and 10 healthy adults. First, a glucose tolerance test with 50 g. of glucose was performed; then within 3 days the test was repeated in the same way except that 10 mg. of prednisolone was given 2 hours before the glucose.

In none of the healthy adults was there a diabetic type of glucose tolerance curve after prednisolone. Of the 14 patients with diseases other than diabetes only one, a girl with Graves's disease, showed a diabetic curve after prednisolone, while only one patient with pancreatic disease showed a diabetic curve with the standard glucose tolerance test, but 4 in this group gave a diabetic curve after prednisolone had been administered. In 2 patients with transient glycosuria and normal or doubtful curves with the standard glucose tolerance test, diabetic curves were observed after prednisolone. In 5 of the patients classified as diabetics there were uncertain abnormalities in the standard glucose tolerance curve; after prednisolone, all 5 showed typical diabetic curves.

The authors conclude that the prednisolone–glucose tolerance test is useful in the detection of the pre-diabetic state and " in the interpretation of borderline standard glucose-tolerance tests ".

K. O. Black

526. **The Small Blood-vessels of the Conjunctiva and Nailbed in Diabetes Mellitus**

J. LANDAU and E. DAVIS. *Lancet* [*Lancet*] **2**, 731–734, Oct. 1, 1960. 4 figs., 14 refs.

The small blood-vessels of the conjunctiva and nailbed were examined in 75 diabetics and compared with those of 140 hypertensive and 110 arteriosclerotic patients, and 65 healthy persons—all aged 40 or more.

Venous congestion in the conjunctiva was found in 60% of the diabetics. The venous limb of the nailbed capillary was also commonly congested. The basic diabetic lesion of capillary congestion on the venous side has thus been found elsewhere than the eye. An arteriosclerotic pattern of the small vessels of the conjunctiva was common in diabetics, and particularly frequent in comparison with the other conditions at ages from 40 to 50. Severe capillary narrowing in the conjunctiva was common, and a high pressure in the terminal digital vessels not uncommon, in diabetics. The incidence of conjunctival micropools in diabetes was appreciable (25%); but although much commoner than in the healthy they were only slightly commoner than in arteriosclerosis and no commoner than in hypertension. Diabetes was associated with characteristic but not pathognomonic changes in the small blood-vessels of the conjunctiva and nailbed.—[Authors' summary.]

527. **Presence of Diabetic Glomerulosclerosis in Patients with Hemochromatosis**

D. BECKER and M. MILLER. *New England Journal of Medicine* [*New Engl. J. Med.*] **263**, 367–373, Aug. 25, 1960. 4 figs., 29 refs.

The clinical records and necropsy findings in 22 cases of haemochromatosis with diabetes and 30 cases of haemochromatosis without diabetes are described in this paper from Western Reserve University School of Medicine, Cleveland, Ohio. In all cases kidney sections were obtained and stained with haematoxylin and eosin and, except in 5 cases, also by the periodic-acid–Schiff technique. Each slide was examined independently by at least four pathologists.

Of the 52 patients only 5 were females, and in these the onset of the disease followed cessation of menstruation. The authors point out that haemochromatosis is predominantly a disease of middle age; in the present series 45 of the 52 patients were between 40 and 70 years of age. Of the 22 diabetics 7 had diffuse glomerulosclerosis and 4 of the 7 also had some nodular glomerulosclerosis. Diabetes had been present for 4 years or longer in all 7 patients and in 2 others without glomerulosclerosis. None of the non-diabetic patients had diffuse glomerulosclerosis.

The authors conclude that diabetic glomerulosclerosis occurs only in patients with both haemochromatosis and diabetes and that its development is in some way directly related to the metabolic defects of the diabetes.

Charles Rolland

528. **Clinical Experiences with Chlorpropamide in Management of Diabetes Mellitus**

E. L. SHLEVIN, H. ZAROWITZ, S. WEISENFELD, and M. G. GOLDNER. *Metabolism: Clinical and Experimental* [*Metabolism*] **9**, 570–579, June [received Aug.], 1960. 1 fig., 12 refs.

The response to treatment with chlorpropamide of 176 patients with mild diabetes of onset in maturity was assessed at the Jewish Hospital and the Jewish Chronic Disease Hospital, Brooklyn, New York. The optimal

daily dose ranged from 200 to 500 mg., but 6 patients required up to 800 mg. daily. Satisfactory clinical control was obtained in 144 patients (82%), but the blood sugar was reduced to normal levels in less than half of these. Blood levels of chlorpropamide fluctuated widely, a minimum of 80 mg. per ml. being necessary to lower the blood sugar level. In 11 patients (6·2%) there were side-effects for which the drug had to be stopped. These consisted of itching, maculopapular eruptions, and abdominal discomfort, in one case the symptoms being associated with abnormal results of liver function tests. In another case liver function tests gave markedly abnormal results and liver biopsy showed pathological changes, but there were no clinical symptoms of hepatic damage and no jaundice. Previous insulin requirement was directly related to therapeutic success, most failures occurring in cases needing more than 30 units of insulin daily. *K. O. Black*

529. **Dimethylguanidine in the Treatment of Juvenile Diabetes** (La dimethylguanidine dans le traitement du diabète infantile)
R. François and A. Ruiton-Ugliengo. *Pédiatrie* [*Pédiatrie*] **15**, 545–561, 1960. 5 figs., bibliography.

The authors first review the literature on the several theories of the mode of action of the oral hypoglycaemic drugs, both the sulphonylureas and the guanidines, and point out that hitherto none of these compounds has been affective in the treatment of diabetes in children. They then report the results in 50 diabetic children, of whom 44 had suffered from the disease for over one year and who, with 2 exceptions, were being treated with insulin. The patients were given dimethylguanidine in a dosage of 50 mg. per kg. body weight, administered in divided doses after meals 2 or 3 times daily. The effect of the drug was assessed by the reduction which could be made in the amount of insulin required to maintain optimum control.

The treatment was considered to have failed in 23 cases, in that after one month the dosage of insulin formerly required could not be reduced by at least 25%. Intolerance, which was usually manifested by gastro-intestinal symptoms, occurred in 18 patients, in whom the drug had to be withdrawn for fear of upsetting the equilibrium and precipitating ketosis. In 9 children, however, the treatment was regarded as successful, since in these patients insulin could either be given up completely or the dosage reduced by 25% or more of the dosage required during the 3 months immediately preceding the administration of dimethylguanidine. Five of these 9 children had had diabetes for more than one year while of the remaining 4 recent diabetics one was a girl in whom the diagnosis had been made on purely routine examination of the urine and who had been well controlled with tolbutamide. In the other 3 the insulin requirements were variable, but in each case it proved possible to treat the patient with dimethylguanidine alone for a minimum of several months.

In 4 children who had been successfully treated with dimethylguanidine alone for at least one week, tests were made to compare the hypoglycaemic action of this drug with that of insulin, with and without the simultaneous intravenous administration of glucose. It was found that 2 g. of dimethylguanidine had a hypoglycaemic action similar to the intravenous injection of $\frac{1}{10}$th of a unit of insulin per kg. body weight; the fall in the blood sugar level, however, was initially slower and more prolonged than with insulin. With small amounts of intravenous glucose the hypoglycaemic effect of dimethylguanidine persisted, but in one case given larger amounts (250 mg. per kg. body weight per hour) its effect was completely blocked. This is interpreted by the authors as indicating that the site of action of dimethylguanidine is hepatic rather than peripheral.

Finally it is reported that so far it has not been found possible to discontinue insulin in any child diabetic for more than one year. *T. D. Kellock*

530. **Some Observations on the Effect of Small Doses of Glucagon in Normal and Diabetic Subjects**
W. J. H. Butterfield, I. Kelsey Fry, and M. J. Whichelow. *Guy's Hospital Reports* [*Guy's Hosp. Rep.*] **109**, 95–109, 1960. 7 figs., 37 refs.

It is suggested that in previously reported studies of the effect of glucagon in human beings the dose of glucagon (10 μg. per kg. body weight) was too high. Preliminary experiments have been carried out which confirmed this and showed that the physiological dose is of the order of 0·5 μg. per kg.

A dose of 40 μg. of glucagon was given by constant intravenous infusion over a period of 20 minutes to 12 healthy controls and 25 diabetics and the response of the blood glucose level was studied.

In the controls there was a prompt, regular rise in the blood sugar level with a peak of 34 mg. per 100 ml. (mean) above the fasting level at the end of the infusion, after which the level fell rapidly. In contrast, the rise in the blood sugar level in the diabetics was delayed and small, with less tendency to fall after the infusion. These abnormalities in the diabetics could not be correlated with any clinical features, but were related to the fasting blood sugar level, patients showing the least response to glucagon "tending to be those with the highest fasting blood-glucose level". The effect of glucagon in 4 mild diabetics after tolbutamide had lowered the fasting blood sugar level was greater than before tolbutamide was given. In those studied the peripheral glucose uptake was not influenced by administration of glucagon.

By analogy with the peripheral tissues, the authors postulate the existence of a glucose threshold in the liver also, its height depending on the availability of insulin. They suggest that the effect of glucagon depends on the level of this threshold and hence on the availability of insulin. It is concluded that tolbutamide does not reduce glycogenolysis but lowers the liver glucose threshold by causing the release of more insulin. The correlation between the response to glucagon and the degree of control—that is, the fasting blood sugar level—suggests that it may be the supply of effective insulin which determines the amount of available liver glycogen.
A. Gordon Beckett

The Rheumatic Diseases

531. **Sydenham's Chorea Without Evidence of Rheumatic Fever: Report of its Association with the Henoch–Schönlein Syndrome, and with Systemic Lupus Erythematosus, and Review of the Literature**
J. L. PARADISE. *New England Journal of Medicine* [*New Engl. J. Med.*] **263**, 625–629, Sept. 29, 1960. 45 refs.

532. **Protracted Relapsing Rheumatic Carditis. Its Association with Chronic Tonsillitis and Its Prevention and Treatment** (Вяло текущий рецидивирующий ревмокардит, его связь с хроническим тонзиллитом и лечебно-профилактические мероприятий)
E. S. MJASOEDOV. *Терапевтический Архив* [*Ter. Arh.*] **32**, 39–43, Aug., 1960. 12 refs.

The author reports the results in 78 patients suffering from rheumatic fever who were followed up after tonsillectomy for 1 to 2 years. Protracted relapsing rheumatic carditis was diagnosed in 37 (47%), while the disease was inactive in 41 (53%); a proportion of the latter group showed evidence of valvular lesions and circulatory failure of Grades I and II. After tonsillectomy 58% of the patients improved, 29% failed to do so, and 13% deteriorated.

Tonsillectomy appears therefore as only one of the measures to be employed in the treatment of acute rheumatism and the author suggests the following course of treatment, which should last 1½ to 2 months: (1) Two 10-day courses of penicillin or tetracycline separated by a 5 days' interval. (2) A search for and elimination of septic foci. (3) Administration of ascorbic acid (0·1 to 0·2 g.), vitamins B_1 and B_2 (0·001 g. of each), and 0·1 g. of vitamin P, all these doses being given 3 times a day for 3 or 4 weeks. (4) Either "pyramidon", 0·24 g. 6 to 9 times a day for 3 or 4 weeks (with frequent blood examinations), or 0·5 g. of aspirin 6 to 8 times a day for 2 to 3 weeks, gradually reducing the dose, or 0·15 g. of phenylbutazone three times a day to a total dose of 18 g. (5) 20 to 40 units of ACTH (corticotrophin) daily up to 1,000 units, or cortisone, 0·025 g. four times daily for 4 weeks. (6) In the absence of circulatory failure small blood transfusions of 75 to 125 ml. every 5 days. (7) Administration of bromides and caffeine to maintain the tonus of the nervous system. If there is circulatory failure treatment should include cardiac supportive therapy, such as tincture of strophanthus, Bekhterev's mixture, or digitalis, and a low-carbohydrate diet, limited salt and fluid intake, and ample calcium. Finally physiotherapy and remedial exercises are given as indicated.

Uniform improvement was achieved in 252 patients thus treated, of whom 87% had valvular disease. The erythrocyte sedimentation rate returned to normal in 55% and was reduced to 10 to 20 mm. in one hour in a further 28%. Since the introduction of the above method of treatment the mean mortality has fallen from 14% (the rate in 1953–4) to 3·1%, and the incidence of subacute bacterial endocarditis has been reduced practically to *nil*. *S. W. Waydenfeld*

CHRONIC RHEUMATISM

533. **Experience with Punch Biopsy of Synovium in the Study of Joint Disease**
G. P. RODNAN, E. J. YUNIS, and R. S. TOTTEN. *Annals of Internal Medicine* [*Ann. intern. Med.*] **53**, 319–331, Aug. [received Oct.], 1960. 5 figs., 21 refs.

The authors of this paper from the University of Pittsburgh School of Medicine, Pennsylvania, report their findings as observed in 142 specimens (from 136 patients) of synovial tissue obtained from knee-joints affected by rheumatic disease by means of the instrument for punch biopsy described by Polley and Bickel (*Ann. rheum. Dis.*, 1951, **10**, 277; *Abstr. Wld Med.*, 1952, **11**, 79). Specimens were taken from three different sites of the suprapatellar bursa distended either with synovial fluid or by the introduction of 40 to 60 ml. of 0·85% sodium chloride solution. The histological appearances were compared with those of 75 specimens taken at necropsy from open knee-joints clinically free from disease. Correlation of "sclerotic atrophy" with advancing age was obtained. The punch biopsy specimens were grouped according to histological appearances into: (1) no disease; (2) non-specific synovitis; (3) questionable rheumatoid arthritis (focal accumulations of lymphocytes, small numbers of plasma cells, minimal oedema, fibrosis, and vascular proliferation, and occasional deposits of fibrin or fibrinoid); (4) rheumatoid arthritis (more pronounced inflammatory focal reaction, prominent number of plasma cells, and, in some cases, pronounced vascular proliferation); and (5) other "specific" types of synovitis (gout, scleroderma, and neuropathic joint disease).

Of 26 patients with rheumatoid disease and active involvement of the knee, the changes in 24 were considered to be "at least in the category of questionable rheumatoid arthritis" and in 17 "were sufficient to place the patients in the category of rheumatoid arthritis". None of the patients with clinically inactive disease gave evidence of active synovitis. Relative acuteness of the inflammatory process was related to the presence of large amounts of fibrin or fibrinoid and numbers of neutrophil polymorphonuclear leucocytes. The authors state that these changes are not specific for rheumatoid arthritis, "being noted as well in cases of systemic lupus erythematosus and psoriatic arthritis. Marked hyaline thickening, atrophy and vascular sclerosis of the synovium were observed in a number of patients with progressive systemic sclerosis (diffuse scleroderma), and are changes

which appear to be pathognomonic of this disease. While urate deposits were detected in the synovium of a number of patients with long-standing gout, the lack of these in many patients with well documented disease (including several with acute gouty geniculitis at the time of biopsy) suggests that tophaceous matter *per se* plays little part in the development of acute gouty arthritis. Punch biopsy of the synovium has proved to be a simple, safe and practical procedure which may supply information of considerable value in the study and diagnosis of joint disease".

There was only one complication of the procedure; a man with myeloma and a bleeding tendency had pain and swelling of the knee which subsided following aspiration of bloody synovial fluid from the distended joint.

Harry Coke

534. **Erythropoiesis in Rheumatoid Arthritis: The Effect of Spleen Extract and Amino Acid Solution on Bone Marrow Cultures.** [In English]
G. HAMMERSTEN, E. JONSSON, G. LINDGREN, A. NERI, E. NETTELBLADT, C. M. PLUM, and B. M. SANDELL. *Acta rheumatologica Scandinavica* [*Acta rheum. scand.*] **6**, 81–91, 1960. 7 refs.

A study of the relationship between spontaneous erythropoietic activity and disease is reported from Södersjukhuset, Stockholm. Samples of bone marrow taken from 54 patients, of whom 23 had rheumatoid arthritis and the remainder various other diseases, were cultured. The cellular layer was obtained by centrifugation and diluted to a count of 30,000 to 50,000 cells per c.mm. This material was divided into 6 separate samples: 2 with added serum from the same patients, 2 with 1% of a splenic extract stated to have an erythropoietic effect (Goldberg *et al.*, *Acta physiol. scand.*, 1950, **22**, Suppl. 77), and another 2 with added amino-acid solution similar in composition to the splenic extract. After 4 to 5 hours' incubation a cell count revealed an increase or otherwise in the number of cells.

No difference in activity was found between the bone-marrow cultures from patients with rheumatoid arthritis and those from patients with other disorders. When, however, splenic extract was added, a significant enhancement of activity occurred in the cultures from cases of rheumatoid arthritis, but not in those from the controls. With the amino-acid solution there was a similar increase in erythropoiesis in cultures from the arthritic group, but results in the other cases were inconclusive.

[Unfortunately, no normal controls appear to have been included in this series.] *G. Loewi*

535. **Large Cysts in Lower Leg Originating in the Knee Occurring in Patients with Rheumatoid Arthritis**
J. P. HARVEY JR. and J. CORCOS. *Arthritis and Rheumatism* [*Arthr. and Rheum.*] **3**, 218–228, June [received Aug.], 1960. 8 figs., 19 refs.

Popliteal cysts communicating with the knee-joint are common in patients with rheumatoid arthritis. Such cysts, which were extensive, reaching well down the calf and lying either between muscles or between muscle and tibia, were seen in 4 patients admitted to the Hospital for Special Surgery, New York, all of whom had had rheumatoid arthritis for some years and had been treated with steroids. Considerable hydrarthrosis was present originally; this was followed later by tender swelling of the calf suggesting thrombophlebitis. The cystic nature of the calf swellings was not always apparent clinically, but arthrograms clearly showed their extent and their communication with the knee-joint. In 3 cases the cysts were excised, with recurrence in 2 and involvement of the other leg later in one. The cyst walls were fibrous without specific cellular lining; in places a palisade-like arrangement of fibroblasts and collections of lymphocytes and plasma cells were seen.

It was uncertain whether the cysts developed by herniation of the synovial cavity of the knee between semimembranosus and gastrocnemius muscles, or by the breaking down of a dividing wall between the joint cavity and a preformed cyst. It is suggested that steroid therapy may have played a part in causing weakness and stretching of the fibrous wall of the synovial cavity and of the cyst. *J. A. Cosh*

536. **Long-term Use of Phenylbutazone in Rheumatoid Arthritis**
R. M. MASON and V. L. STEINBERG. *British Medical Journal* [*Brit. med. J.*] **2**, 828–830, Sept. 17, 1960. 2 figs., 9 refs.

The results of long-term administration of phenylbutazone to 315 patients with rheumatoid arthritis and the findings at the end of 4 years are described in this paper from the London Hospital. In the majority of patients the dosage ranged from 100 to 400 mg. daily, but of 12 who had up to 1,200 mg. daily for short periods 2 developed intolerance to the drug. In some cases treatment brought about a remission and in others it was ineffective. At the end of 3 months the drug was discontinued in 37% of the patients, after 2 years in 80%, and after 3 years in 88%. Intolerance was the commonest reason for discontinuing the drug, particularly in the early stages of treatment. Symptoms of intolerance were observed in 15·9% of the patients during the first 3 months and in only 27·7% at the end of 3 years; after 3 years no further cases of intolerance were encountered. Gastro-intestinal symptoms and rash were the commonest toxic manifestations, but stomatitis, oedema, and blood dyscrasias were also observed. At the end of 3 months, 198 of the patients were taking phenylbutazone, 7 of them being in remission; at the end of 2 years, the figures were 62 and 2 respectively, and at the end of 3 years, 45 and 0 respectively. The number of patients in whom the drug was ineffective and therefore withdrawn was 90 in the first 3 years and 3 in the fourth year; only 38 patients continued to take the drug after 4 years. The incidence of remission was highest between the 6th and 24th months of treatment, but some remissions were observed up to 3 years. The authors consider that the longer the patient takes phenylbutazone, the less likely is the development of intolerance. They regard this as an indication for continuing treatment for a long time in the hope of achieving a remission and avoiding steroid therapy with its very toxic effects. *William Hughes*

Neurology and Neurosurgery

537. **Cerebrospinal Fluid Gamma-globulin in Multiple Sclerosis: Observations on Its Nature**
E. J. FIELD and A. RIDLEY. *British Medical Journal* [*Brit. med. J.*] **2**, 1053–1055, Oct. 8, 1960. 9 refs.

It has been suggested that the presence of excess γ-globulin in the cerebrospinal fluid (C.S.F.) of patients with disseminated sclerosis points to this being an autoimmune disease, and the authors have examined this theory at the Royal Victoria Infirmary, Newcastle upon Tyne, using the antiglobulin consumption test introduced by Steffen (*Wien. Z. inn. Med.*, 1954, **35**, 422). C.S.F. globulin was allowed to react with Coombs anti-human-globulin serum, and the amount of the latter removed by combination with the former was measured by the final dilution capable of agglutinating sensitized human erythrocytes. Before the test was performed the C.S.F. was further allowed to react with brain-tissue emulsion, both from normal subjects and from patients with disseminated sclerosis, and it was found that no removal of γ-globulin occurred as judged from the subsequently performed antiglobulin consumption test. It is probable, therefore, either that the C.S.F. γ-globulin is not antibody globulin, or that brain tissue is not its responsible antigen. The authors favour the former interpretation and suggest that the excess C.S.F. γ-globulin in disseminated sclerosis may be derived from the breakdown of nervous tissue.

J. B. Cavanagh

538. **Phenytoin in the Treatment of Trigeminal and Other Neuralgias**
J. BRAHAM and A. SAIA. *Lancet* [*Lancet*] **2**, 892–893, Oct. 22, 1960. 7 refs.

Phenytoin (diphenylhydantoin) in a dosage of 0·1 g. 3 times daily was given by mouth to 20 patients with trigeminal neuralgia at the Tel-Hashomer Government Hospital, Israel. Relief was complete in 8 patients (including one with disseminated sclerosis) and partial in 6, but in the remainder there was no effect. Lightning pains in 2 tabetics, and paroxysmal pains in 2 cases of post-herpetic neuralgia, were also relieved by phenytoin. The authors suggest that phenytoin should always be tried before alcohol injection or surgical division is contemplated in trigeminal neuralgia. *I. Ansell*

539. **Neurosurgical Alleviation of Intention Tremor of Multiple Sclerosis and Cerebellar Disease**
I. S. COOPER. *New England Journal of Medicine* [*New Engl. J. Med.*] **263**, 441–444, Sept. 1, 1960. 5 refs.

The author has had unique experience in the alleviation of resting tremor and rigidity in Parkinson's disease by creating destructive lesions in the globus pallidus and thalamus. More recently he has found that the same procedure has relieved the movement disorders of dystonia. In the course of this work it was noticed that intention tremor as well as resting tremor was relieved by means of a lesion placed in the ventrolateral nucleus of the thalamus by the technique of chemopallidectomy. In this paper from New York University Medical Center and St. Barnabas Hospital, New York, he reports the results obtained in 12 patients with incapacitating intention tremor treated in this way. The causes of the tremor were trauma in 2 cases, disseminated sclerosis in 6, familial cerebellar degeneration in 2, cerebellar degeneration of uncertain aetiology in one case, and olivocerebellopontine degeneration in one. The ages of the patients ranged from 20 to 68 years, and the duration of symptoms from 3 to 30 years. The surgical technique was the same as that used for the relief of Parkinsonian tremor. It is emphasized that in this small series of cases, the position of the effective lesion appeared to vary from case to case. It therefore appears essential initially to provide a temporary or reversible lesion that can be tested before a permanent lesion is created. In 10 of the 12 cases practically complete relief was obtained; there was only partial alleviation in one case and in one a pre-existent spastic hemiparesis was aggravated by the procedure.

The findings would appear to establish that severe intention tremor, however caused, can be abolished or mitigated by inflicting a destructive lesion in the ventrolateral nucleus of the thalamus on the opposite side.

J. V. Crawford

540. **Cervical Disk Lesions with Neurological Disorder. Differential Diagnosis, Treatment, and Prognosis**
A. M. G. CAMPBELL and D. G. PHILLIPS. *British Medical Journal* [*Brit. med. J.*] **2**, 481–485, Aug. 13, 1960. 1 fig., 22 refs.

The management of 60 cases of myelopathy or radiculitis associated with cervical intervertebral disk lesions seen at Frenchay Hospital, Bristol, is discussed. The authors state that much of the confusion concerning the treatment of cervical spondylosis is due to failure to distinguish the main types of lesion; they recognize and describe four types.

1. Cervical spondylosis with myelopathy (33 cases). The authors state that cases of this type are the most difficult to treat and the results of treatment difficult to assess. In the early years treatment was by operative decompression, particularly if symptoms were severe, but few operations were performed later because of the continued success of conservative measures; this change in policy followed unexpected improvement in 2 patients with severe disability who were awaiting operation. Conservative treatment consisted in the application of a modified Minerva plaster-type collar, which was worn for 3 months, and then of a short plastic collar which was worn for 3 to 6 months. Of 26 patients treated in this way 20 were working after 2 years, but in those in whom symptoms had been present more than a year improvement was limited.

2. Cervical spondylosis with brachial neuritis (12 cases). The satisfactory results obtained with the modified Minerva collar led to operation being abandoned for patients with this type of lesion.

3. Prolapsed cervical nucleus pulposus (6 cases). Myelography was carried out in 4 of these and, later, operation in all 6 with a satisfactory relief of symptoms in 5.

4. Coincidental cervical spondylosis and cervical myelopathy (9 cases). Of the 9 patients 4 were found to be suffering from disseminated sclerosis and 3 from motor neurone disease. In one patient a cervical extradural sarcoma was found at necropsy 2½ years after operation for spondylosis and in one diffuse cerebral degeneration developed 2 years after cervical laminectomy.

[The importance of this paper lies in the emphasis placed upon the differentiation of the lesions and in the really excellent results achieved by adequate immobilization of the neck in plaster.] *J. V. Crawford*

DIAGNOSTIC METHODS

541. **The Phylo- and Onto-genic Analysis of Muscular Control in the Spastic Hemiplegias.** (Фило- и онтогенетический анализ мышечной установки при спастических гемипарезах)
V. A. KARLOV. *Журнал Невропатологии и Психиатрии* [*Ž. Nevropat. Psihiat.*] **60**, 947–952, No. 8, 1960. 3 figs., 20 refs.

The author presents observations based on the study of 60 children and 37 adults with cerebral hemiparesis, 18 of the children having severe hemiplegia with marked pyramidal signs. He points out that the limb posture of these children and especially of the youngest infants differs from that of adults, this difference consisting in greater flexion and pronation of the forearm, flexion and ulnar deviation of the wrist, and a more extreme equinovarus position of the foot. In young infants flexion and external rotation of the hip, flexion of the knee, and abduction of the shoulder are the rule, that is, a quite different posture from that of adults, the big toe being abducted and the others flexed.

This difference in posture the author regards as being due to a reversion to the antigravitational reflexes of the evolutionary ancestors of man; thus the infant reverts to the posture of the tree-dwelling lemuroids and the older child to that of the anthropoids. The younger the child, the further back in the evolutionary scale is the recession, since the infant has not yet developed the antigravitational reflexes required by the upright human posture. Sketches of present-day lemuroids and anthropoids are presented to illustrate the normal posture necessarily adopted by these animals to maintain them in their habitual relation to gravity. These reflexes are altered at the cerebral level in man to enable him to stand in the normal upright posture; but with the destruction of the higher motor centres the hemiplegic posture reverts to that imposed by the phylogenetically older, and lower, centres. Thus, the pronation of the wrist brings the hand into the position required by the ape for partial support of the body. The author states that young children learning to walk tend to take up this posture at first. Extension and supination of the forearm are movements required in the use of the upper limb for human activities, as is also the opposition of the thumb. These movements are severely impaired in the hemiplegic child. *L. Firman-Edwards*

542. **Eserine Activation of the EEG in Children**
I. LESNÝ and V. VOJTA. *Electroencephalography and Clinical Neurophysiology* [*Electroenceph. clin. Neurophysiol.*] **12**, 742–744, Aug., 1960. 15 refs.

It is pointed out that the use of leptazol to activate the electroencephalogram (EEG) in children is inadvisable because of the danger of provoking seizures. In this paper from Charles University, Prague, the authors report a trial of physostigmine in 71 children in whom epilepsy was suspected and a routine EEG showed no epileptiform activity. The history suggested that 54 had centrencephalic epilepsy and the remainder cortical epilepsy. The drug was given in a 1 in 1,000 solution in a dosage of 0·15 to 0·2 ml. to children under 6 years and 0·25 to 0·35 ml. to children over that age but under 15 years. The EEG was recorded for half an hour after the injection and overbreathing was carried out as a routine.

Spikes or spikes and slow waves appeared in 22 tracings and "episodic synchronous slow activity", which the authors regarded as specifically epileptiform, in 19. In many others there was a generalized increase in slow activity, but only in 8 was the EEG unaffected. Of 18 healthy children 4 showed slowing of the rhythm after physostigmine but no epileptiform activity. Spikes were provoked in only one out of 12 adult epileptics with non-specific routine EEG tracings.

[The figures given in the tables differ from those in the text.] *L. G. Kiloh*

BRAIN AND MENINGES

543. **Psychological Studies on the Effects of Chemosurgery of the Basal Ganglia in Parkinsonism. II. Aspects of Personality**
M. RIKLAN, L. DILLER, and H. WEINER. *Archives of General Psychiatry* [*Arch. gen. Psychiat.*] **3**, 267–275, Sept., 1960. 41 refs.

Fifty-one Parkinsonians undergoing chemosurgery were administered the Rorschach test preoperatively (mean time=4·6 days), postoperatively (mean time=18·5 days), and in a long-range postoperative situation (mean time=9 months and 27 days). The outstanding immediate postoperative changes for the total group in the "structure of personality" were a generalized diminishment in productivity or drive combined with losses in perceptual integration. A more specific finding was a significant decrease in those aspects of personality which might be referred to as more primitive and appeared more pronounced in patients undergoing left hemisphere surgery. Several explanatory suggestions were offered

for this finding, and an attempt was made to integrate them into an hypothesis concerning the role of subcortical structures in personality. In the long-range situation, while some trends for the total group continue in the direction of diminished general reactivity, and limitation in perceptual accuracy, the most significant finding is an increase in emotional expansion reflected primarily in the right-brain group. It was suggested that a combination of physiologic and psychologic factors might be operating. Thalamic lesions seem more disruptive than others immediately postoperatively, though not in long-range assessment. To some degree older patients return more slowly to preoperative levels of functioning.—[Authors' summary.] [See also *Abstr. Wld Med.*, 1960, **28**, 151.]

544. **After-effects of Brain-injuries: Research on the Symptoms Causing Invalidism of Persons in Finland Having Sustained Brain-injuries during the Wars of 1939–1940 and 1941–1944.** [Monograph, in English]
E. HILLBOM. *Acta psychiatrica et neurologica Scandinavica* [*Acta psychiat. scand.*] **35**, Suppl. 142, 1–195, 1960. Bibliography.

545. **The Use of Profound Hypothermia, Extracorporeal Circulation and Total Circulatory Arrest for an Intracranial Aneurysm: Preliminary Report with Reports of Cases**
A. UIHLEIN, R. A. THEYE, B. DAWSON, H. R. TERRY JR., D. C. MCGOON, E. F. DAW, and J. W. KIRKLIN. *Proceedings of the Staff Meetings of the Mayo Clinic* [*Proc. Mayo Clin.*] **35**, 567–576, Sept. 28, 1960. 8 figs., 11 refs.

The surgical approach to aneurysms of the anterior communicating artery is difficult because of haemorrhage. At the Mayo Clinic a technique of profound hypothermia, extracorporeal circulation, and total circulatory arrest was used during surgical treatment of 2 patients with leaking aneurysm of the anterior communicating artery. An extracorporeal circulation for the left heart leading from a catheter in the left atrium to a cannula in the right external iliac artery and a further extracorporeal circulation for the right heart leading from a catheter in the right atrium to a catheter in the pulmonary artery were set up. The blood in the left heart circulation was then cooled by a heat exchanger, the body temperature decreasing at a rate of 1·5° C. a minute. As the body temperature fell the by-pass circulation of the right heart was also switched on. When the body temperature had fallen to between 25° and 30° C., cardiac fibrillation or stand-still occurred. High blood flows were continued until the body temperature reached approximately 15° C., at which level the temperature was stabilized. In this condition the patient was able to withstand circulatory arrest—obtained simply by stopping the extracorporeal pumps—for 30 to 60 minutes during the neurosurgical operation. After the operation had been completed, the whole process was reversed and cardiac defibrillation was accomplished in the usual way when body temperature had reached 38° C. Throughout the procedure of by-pass, the patient received heparin in a dosage of 90 mg. per square metre body surface.

In the first patient a severe left hemiplegia developed and he died on the third postoperative day. The second patient had a satisfactory postoperative course and showed no physical or mental defects which could be attributed to the surgical procedure. *J. B. Stanton*

546. **Occlusion of Intracranial Venous Structures: a Consideration of the Clinical and Electroencephalographic Findings**
H. LEMMI and S. C. LITTLE. *Archives of Neurology* [*Arch. Neurol.*] **3**, 252–266, Sept., 1960. 12 figs., 37 refs.

547. **Drug Prophylaxis in Migraine: a Controlled Clinical Trial**
R. GRAHAME. *British Medical Journal* [*Brit. med. J.*] **2**, 1203–1207, Oct. 22, 1960. 28 refs.

The author investigated the relative merits of reserpine and of phenobarbitone in controlling attacks of migraine by comparing the effect of these drugs with that obtained with a placebo and with no treatment at all. The trial was carried out at the Cambridge Military Hospital, Aldershot, on 28 patients whose attacks of migraine were frequent. In the first half of the trial their response to reserpine, 0·25 mg. 3 times a day for 6 weeks, was compared with that to an identical inert tablet for a similar period. Random selection with cards determined whether the patient started with reserpine or with the inert tablets. For a third period of 6 weeks phenobarbitone, ½ gr. (32 mg.) 3 times a day, was given, and this was followed by a 6-week period without any maintenance therapy. The response to reserpine and to phenobarbitone was favourable in 14 and 11 cases respectively. Of 15 patients not improved by phenobarbitone, 5 were improved by reserpine; and of 14 not helped by reserpine, 3 improved with phenobarbitone.

[As the author remarks, in this series there was a marked preponderance of men (93%) and all the patients were having very frequent attacks.]

J. W. Aldren Turner

548. **The Role of the Age Factor in the Clinical Picture of Epileptic and Epileptiform Symptoms in Children. I. Purposive Convulsions.** (О роли возрастного фактора в картинах эпилептических и эпилептиформных проявлений у детей. Сообщение I. О выразительных судорожных пароксизмах у детей)
S. S. MNUHIN. *Журнал Невропатологии и Психиатрии* [*Z. Nevropat. Psihiat.*] **60**, 846–851, No. 7, 1960. 10 refs.

In the author's opinion one of the barriers to the solution of the problem of epilepsy is the unsatisfactory existing classification of epileptiform attacks. For example, the use of the terms " motor " and " psychic " is an oversimplification, and those such as major, minor, abortive, and similar terms are purely symptomatic, while he deprecates narrowly anatomical differentiation, such as cortical or mesencephalic. He prefers to attempt an approach from the clinico-physiological angle and, following the principles of Speransky and of Ivanov and Smolensky, to regard epileptic fits as expressions of diverse complicated automatic movements and as a

series of stages in the " functional and genetic hierarchy " of self-defensive mechanisms.

On these lines he has analysed a series of 588 children and adolescents aged from one to 16 years suffering from various types of epilepsy. He distinguishes two main types: (A) the complicated " expressive " or " differentiated " paroxysm, and (B) the simple elementary or true epileptic fit. Of his patients, 91 showed in their symptom-picture, especially in the first years of the disease, most of the characteristics of main type A, which he divides into three sub-types: (1) momentary and head-nodding attacks, (2) systematically repeated status epilepticus, and (3) expressive tonic attacks, describing these more fully as follows.

(1) Thirty-five patients (6% of the total) exhibited movements suggestive of self-defence mechanisms, as seen in infants suffering from fear or in children with Little's disease. This type usually appears about the age of one year and rarely after the age of 3, and is often (22 of these 35 cases) associated with a history of intra-uterine noxa or pathological birth. In some children it develops on a background of microcephaly or severe congenital or early acquired psychic and motor insufficiency. In the course of time it progresses to severe tonic or major epilepsy, with attacks of status epilepticus. It does not usually respond to anticonvulsant therapy.

(2) In 35 cases (6%) the disorder was characterized by bouts of status epilepticus over a course of years or months; this type occurs mostly in boys (23 of the 35 cases) up to 3 years of age. These bouts are not a series of simple attacks, for the convulsive movements are prolonged, systematized, and purposeful. They may last for 24 hours or more and recur at intervals varying from a few weeks to several years. Tonic contractions often predominate and are accompanied by symptoms of vegetative nervous activity (sweating, vomiting, or diarrhoea) and the picture may simulate acute cerebral inflammation. In this type, as in the first, there is often a history of prenatal or birth trauma, but in addition there may be a background of endocrine-vegetative disturbance, such as sexual precocity, adiposity, or ichthyosis. This type also responds poorly to medication, but in 2 cases disappeared spontaneously after several years.

(3) In this third type tonic expressive attacks are of subcortical origin; they occur chiefly in boys (17 of 21 cases in this group), begin rather later than in the other two types, usually between 5 and 7 years of age, are not associated with prenatal or birth trauma, and may occur on a normal psychic and motor background. They are very varied in their manifestations and differ from Types 1 and 2 in their complex and purposeful posturing and strong emotional colouring. The poses adopted, essentially self-defensive in nature, consist in attempts to grasp something or to sit up from the lying position; but on the other hand they may simulate a cataleptic stupor. The attacks occur in bouts, becoming more and more frequent over a period of days or weeks, and then diminishing in frequency, while between these bouts long intervals, even years, may elapse. In a minority of cases (7 of the present group) these systematized tonic attacks are associated with other fits, especially of Type 1, or (rarely) with generalized convulsions. The commonest time for these attacks to occur is on waking or when going to sleep. They are frequently followed by periods of psychomotor inhibition, with muscular hypotonia; symptoms of Parkinsonism and rigidity may ensue later. This type, like the others described, also responds poorly to medication. *L. Firman-Edwards*

PERIPHERAL NERVES

549. **Mental Disturbances in von Recklinghausen's Disease.** (О нарушениях психики при болезни Реклингаузена)

A. A. Volkov. *Журнал Невропатологии и Психиатрии* [*Ž. Nevropat. Psihiat.*] **60**, 887–890, No. 7, 1960. 2 figs., 31 refs.

The mental disturbances in Recklinghausen's disease (neurofibromatosis) have been but scantily described in the literature. The author therefore presents the case of a boy, who at the age of 2 years, one month after having had measles, developed severe headaches, unsteady gait, speech defects, squint, poor vision, facial asymmetry, bulimia, and polydipsia. In a short while the child became obese and also restless, capricious, and irritable. At the age of 5 he had one severe epileptiform seizure of grand mal type, but thereafter had no further such attacks. The history showed that his paternal grandmother died young of an obscure disease characterized by obesity and polydipsia, and that his father had an abortive form of neurofibromatosis, with pigmented patches on the skin and slight mental defect. The boy came under the author's observation at the age of 8. At this time he had numerous pigmented patches all over the body and a tumour on the right shoulder measuring 5×4 cm. and covered with thickened, hairy skin, while a smaller tumour was present on the upper lip and a few on the scalp. The patient's head was enlarged (circumference 59 cm.) and he had syndactyly of the toes.

Craniography showed that there was thinning of the vault and a bone defect at the base, anterior to the sella turcica, oval in shape, and 10 mm. long. Pneumoencephalography revealed imperfect filling of the cerebral ventricles and hydrops of the lateral ventricles, with widening of the subarachnoid space on the brain surface. In the electroencephalogram the frontal leads showed clearly marked gigantic slow waves at 2 to 3 per second, spike waves of rapid rhythm were seen in the frontal and temporal leads and disappeared on closing the eyes, while parietal unipolar leads showed delta rhythm at 4 to 7 per second. Mentally the boy was apathetic; when left to himself he monotonously sorted cube-blocks. He was polite and good-natured with his fellow-patients, and when with adults he asked innumerable naïve questions, wanted to measure his strength with them, and to show off how he could jump. Attempts to teach him the alphabet for the blind were unsuccessful. Left to his own devices he was helpless, clumsy, and untidy. The evidence pointed to neurofibromatosis in the region of the optic chiasma, with involvement of the frontal lobes. *L. Firman-Edwards*

Psychiatry

550. **Confusion in the Elderly: Some Common Remediable Causes**
K. L. G. Nobbs. *Lancet* [*Lancet*] **2**, 888–889, Oct. 22, 1960. 3 refs.

Confusional states arise in the elderly during relatively minor disorders. It is assumed that cerebral vascular disease leaves them with a narrow margin of reserve. Some causes of transient confusional states are reviewed, and 2 or 3 cases illustrative of each are briefly described. Among the commonest causes are a bowel loaded with impacted faeces, perhaps also associated with spurious diarrhoea, and anaemia, even of mild degree; it is claimed that mental recovery follows treatment of the anaemia if this has not persisted too long. Simple dehydration may be a cause of confusion, especially when it is associated with salt depletion, malnutrition, or vitamin deficiency. Bronchopneumonia, cardiac infarction, diabetic gangrene, and uraemia are other causes. The author emphasizes the need in the elderly for rectal examination and early detection of bronchopneumonia, which is often apyrexial, symptomless, and productive of few signs.

[These facts are well understood in geriatric medicine, but deserve wider general recognition.] *J. N. Agate*

551. **A Trial of Discharge and Aftercare of Long-stay Mental Hospital Patients**
J. C. N. Tibbits and W. B. Harbert. *British Medical Journal* [*Brit. med. J.*] **2**, 436–438, Aug. 6, 1960. 4 refs.

The authors describe from All Saints Hospital, Birmingham, a detailed investigation of 223 male long-stay mental patients and their attempts to discharge as many of them as possible from hospital. Previous investigations by Cross *et al.* (*J. ment. Sci.*, 1957, **103**, 146 and by Garratt *et al.* (*Brit. J. prev. soc. Med.*, 1957, **11**, 165; *Abstr. Wld Med.*, 1958, **23**, 459) had revealed that only social difficulties prevented the discharge of at least 12% of such patients. All the authors' patients had been treated with drugs and other physical methods as well as by social and occupational therapy. The second-named author, who is a psychiatric social worker (P.S.W.) to the City of Birmingham Public Health Department, helped in gaining the cooperation of the patients' relatives, and visiting by these and periods of home leave were encouraged. Each patient was interviewed and his condition assessed by a doctor, while the P.S.W. and a clinical psychologist gave advice on vocational guidance. The patient was helped over his initial anxieties about discharge by discussions with the P.S.W., who continued to offer help and support after discharge. When regular home leave had led to no difficulties the patient was discharged, but allowed to attend hospital daily if no employment could be found. Ability to be employed was an important factor in a patient's discharge. Many long-stay patients had no homes to return to and it was difficult to find landladies willing to accept discharged mental patients. Some patients could live outside hospital if they had a supportive community, such as a hostel, to return to.

Of a total of 38 patients who were discharged 28 remained outside hospital, but the other 10 had to be re-admitted. During the 6-year period 1953–8 only 86 long-stay male patients were discharged. The records showed that in spite of recent improvements in therapy, together with efforts at rehabilitation, no great increase in the numbers leaving hospital had been effected. It was shown that the great majority of patients were unable to leave hospital because of their mental condition, but it is considered that probably some 20% could be discharged if hostels were available in which the patient's transition to normal life could be made easier. It is concluded that this inquiry illustrates the need for the P.S.W. to establish contact with the patient before he leaves hospital, while the number of re-admissions emphasizes the need for follow-up and after care.

M. R. Medhurst

552. **Metabolic and Cardiovascular Changes during a State of Acute Central Nervous System Arousal**
M. D. Bogdonoff, E. H. Estes, W. R. Harlan, D. L. Trout, and N. Kirshner. *Journal of Clinical Endocrinology and Metabolism* [*J. clin. Endocr.*] **20**, 1333–1340, Oct., 1960. 5 figs., 16 refs.

Measurements of plasma free fatty acid (FFA) and glucose levels, urinary excretion of adrenaline and noradrenaline, heart rate, and blood pressure were made in 20 students undergoing a major 15-minute scholastic examination. Similar measurements were made on a non-test day. Marked increases in plasma FFA concentration occurred in all 20 students during the examination. Plasma glucose concentration also rose. The urinary excretion of adrenaline increased in all subjects. Urinary excretion of noradrenaline varied sporadically. The heart rate increased in all. Several students had marked tachycardia (120 to 166 beats per minute). Independent post-examination assessment of affect arousal indicated varying degrees of response. A rating of affect arousal was correlated to some extent with the level of the heart rate and with the magnitude of the increases in serum FFA and glucose levels and in the urinary excretion of adrenaline. These acute changes suggest that lipolysis may be a companion process to glycogenolysis as part of the organism's response to arousal.—[Authors' abstract.]

553. **Rosacea and Morbid Reddening: Some Psychoanalytic Aspects**
E. Plesch. *Psychosomatic Medicine* [*Psychosom. Med.*] **22**, 377–390, Sept.–Oct., 1960. 21 refs.

The psychodynamic problems underlying rosacea and the allied condition of morbid facial reddening are discussed with reference to psychoanalytic observations in 5 female patients treated for 9 months to 3 years, with

follow-up interviews over periods up to 15 years. Some of the findings were confirmed in a further group of 15 females who were interviewed.

The dominant psychodynamic theme in all 5 patients was a profound identification with the father. In most instances another key figure within the family subsequently became an object of paternal identification, but when this object of identification was ultimately lost the skin condition began. At a deeper level, analysis disclosed considerable emotional difficulty between the patients and their mothers, the latter being profoundly disturbed individuals. In this connexion deep unsatisfied oral cravings were revealed by the patients.

The problem of rosacea and blushing is considered and discussed in a biological context. The exhibitionist impulses associated with rosacea are held to be analogous to display activities in primitive peoples and in animals. It is suggested that reddening represents the survival of a primitive defence mechanism. [The restriction of this investigation to female patients limits any generalizations arising therefrom.] *A. Balfour Sclare*

554. **" Climbing Movements " in the Final Stages of a Case of Alzheimer's Disease.** (Über das Auftreten von " Kletterbewegungen " im Endstadium eines Falles von Morbus Alzheimer)
G. PILLERI. *Archiv für Psychiatrie und Nervenkrankheiten* [*Arch. Psychiat. Nervenkr.*] **200**, 455–461, 1960. 4 figs., 18 refs.

From the Psychiatric Clinic, Waldau–Berne, the author describes the case of a 72-year-old patient in the final stages of Alzheimer's disease who showed the grasp reflex, automatic sucking movements, and also movements like those of climbing. When the grasp reflex and the sucking reflex were elicited simultaneously the former appeared to be markedly reinforced, thus illustrating Lorenz's law of summation of stimuli. The climbing movements are considered to be homologous to certain movements seen in the human baby and in the newborn monkey, the latter in particular showing this type of motor behaviour when holding on to its mother's fur. The reappearance of this movement in the later stages of cerebral disease is explained in terms of Jackson's law of disintegration of function of the central nervous system. *J. Hoenig*

555. **Psychiatric Syndromes of Endogenous Type in Cerebrovascular Disease.** (Endoforme Psychosyndrome bei cerebralen Durchblutungsstörungen)
V. ALSEN. *Archiv für Psychiatrie und Nervenkrankheiten* [*Arch. Psychiat. Nervenkr.*] **200**, 585–602, 1960. 12 refs.

From the University Neurological Clinic, Münster, are described 23 male patients (that is 5·5% of all male admissions during the years 1957–8) who, although presenting the clinical picture of endogenous psychosis, were also suffering from cerebrovascular disease. The patients were all over 40 years of age. The author concludes that in these cases the clinical picture is determined by a psychotic disposition which is, as it were, activated by the cerebrovascular disease. While agreeing that this view is purely speculative, he nevertheless considers that such patients are worth considering as a special group for the purpose of further research. *J. Hoenig*

556. **The Obsessive-compulsive Chronic Alcoholic**
E. PODOLSKY. *American Journal of Psychiatry* [*Amer. J. Psychiat*]. **117**, 236–238, Sept., 1960.

The author attempts to demonstrate the clinical similarities of the obsessive-compulsive neurotic and the obsessive-compulsive chronic alcoholic. He refers to some of the mechanisms and clinical features of the obsessive-compulsive alcoholic and their resemblance to those observed in patients with obsessive-compulsive neurosis. The obsessive-compulsive drinker, usually of middle age, resorts to alcohol to mitigate his anxieties, inner tensions, and guilt feelings and to lessen the pressure of ritualistic behaviour and obsessive thoughts. Among the permanent features of these alcoholics are obsessive fears, rituals, rigidly controlled emotional reactions, hypochondriacal trends, and pseudo-attempts at suicide and homicide.

The author then describes 6 patients whose case histories illustrate some of the above features. He considers that psychotherapy directed to strengthening the patient's ego and modifying his defences, and administration of tranquillizing drugs to mitigate the need for alcohol are effective in the treatment of such patients. *N. H. Rathod*

557. **The XXX Syndrome: Frequency among Mental Defectives and Fertility**
J. H. FRASER, J. CAMPBELL, R. C. MACGILLIVRAY, E. BOYD, and B. LENNOX. *Lancet* [*Lancet*] **2**, 626–627, Sept. 17, 1960. 1 fig., 9 refs.

The incidence of the XXX chromosome complement in female mental defectives was studied in 637 such patients at Lennox Castle Mental Deficiency Hospital, Stirlingshire. Examination of buccal mucosal smears revealed that 4 patients had an XXX chromosome complement. The ages of the patients ranged from 30 to 73 years and the age of the mother when the patient was born from 28 to over 40 years. The I.Q. ranged from 38 to 50. The percentage of nuclei with single sex chromatin varied from 33 to 66 and the percentage with double sex chromatin from 25 to 33. The nodal chromosome number was 47 in each case. All the patients had Group-A blood and were epileptic, but there were no striking clinical features. The menstrual history was normal or near normal in 3 patients and one of these gave birth to a physically normal male child of average intelligence with chromatin-negative smear and 46 normal chromosomes.

It is suggested that the incidence of the XXX syndrome in the general population is lower than 0·7%, that the extra X chromosome produces no clinical effect but must be responsible for the mental deficiency, and that the fact that all the patients were epileptics and of blood-group A might be coincidental. [No evidence is advanced for this last statement. If the extra X chromosome is responsible for the mental deficiency it is producing a clinical effect.] *G. de M. Rudolf*

558. **Changes in Porteus Maze Scores of Brain-operated Schizophrenics after an Eight-year Interval**
A. SMITH. *Journal of Mental Science* [*J. ment. Sci.*] **106**, 967–978, July [received Oct.], 1960. 43 refs.

After an interval of 8 years the author has re-examined 50 of the 68 chronic schizophrenic patients who had taken part in the original project of the New York State Brain Research (*Studies in Topectomy*, New York, 1956) and were still at this time inmates of Rockland State Hospital. All the patients had a poor prognosis; 31 were aged between 36 and 48 (average 42) years at the time of re-examination and 19 between 54 and 66 (average 59) years. Topectomy had been performed on 27 patients, while 23 had been members of the unoperated control group which had been carefully matched on a large array of variables. A superior topectomy, with bilateral excision of Brodmann areas 9, 8, and 32, had been carried out on 12 of the younger group and 5 of the older group, and an orbital topectomy, with bilateral excision of Brodmann areas 11 and 10 and Walker's area 13, on 7 young and 3 old patients.

The Porteus Maze test has proved the most sensitive psychological indicator of postoperative brain disturbance. All the patients treated surgically had shown an initial, but temporary, reduction of test scores, in contrast to the controls, whose test scores tended to increase through practice.

It had been generally assumed that there would be no long-term postoperative defect of brain function. The author found, however, that after 8 years this was true only for young patients subjected to orbital topectomy. Both young and old patients subjected to superior topectomy showed a marked decrease in scores at the end of this period. This was also the case in 3 old patients treated by orbital topectomy. It is pointed out, however, that the small number of patients makes this last result doubtful, though it may be significant as the 3 patients also had poor scores on 4 additional tests.

The author is of the opinion that the long-term reduction of Porteus Maze test scores may be the psychological analogue of neuro-anatomical changes due to secondary degenerations which had been found by other investigators to be positively correlated with the length of time after operation, the site of the brain operation, and the age of the subject at the time of surgical intervention.

F. K. Taylor

TREATMENT

559. **Drug Therapy in Child Psychiatry: Pharmacological Aspects**
B. FISH. *Comprehensive Psychiatry* [*Comprehens. Psychiat.*] **1**, 212–227, Aug., 1960. 21 refs.

It is pointed out that the value of drugs in the treatment of psychiatric illness in children is difficult to assess and the interpretation of the response to a particular drug presents the same problem as in the adult. In this paper from Bellevue Hospital, New York, a study is reported of 85 children, aged 1 to 12 years (schizophrenia in 28, organic brain disease in 6, and primary behaviour disorders in 51) who were given drugs as one part of their total out-patient treatment. All had been subjected to psychiatric and neurological examinations during the 4-week period preceding treatment.

Such factors as motor, language, and social development as well as anxiety and apathy were assessed and rated. Amphetamine diphenydramine, chlorpromazine, prochlorperazine, perphenazine, and trifluoperazine were given at various dose levels. There were no placebo controls, the relative efficacy of the different drugs being directly compared. Toxic effects were not a problem. It was found that on the whole administration of drugs was a useful adjuvant in the treatment of these patients. The phenothiazine derivatives (particularly trifluoperazine) were effective over the entire spectrum of clinical disturbances studied, while amphetamine was useful only in " neurotic " behaviour disorders.

[More controlled studies are needed before any firm conclusions can be drawn concerning the value of drugs in the treatment of psychiatric illness in children.]

B. M. Davies

560. **Treatment of Severe Depression by Imipramine (Tofranil): an Investigation of 100 Cases**
D. BLAIR. *Journal of Mental Science* [*J. ment. Sci.*] **106**, 891–905, July [received Oct.], 1960. 1 fig., 16 refs.

In this paper is described the response to imipramine of 100 women with severe depression, all in-patients at St. Bernard's Hospital, Southall, Middlesex. The classic features of the depressive syndrome are described and applied to 6 defined types of illness: manic-depressive, endogenous, senile arteriosclerotic, psychoneurotic, psychopathic, and schizo-affective. The value of imipramine was also assessed from 4 other viewpoints: patients unsuitable for further electric convulsion therapy (E.C.T.); those inadequately responsive to E.C.T.; those previously treated with E.C.T.; and those experiencing their first attack of depression. The patients were adults of all ages and the duration of the illness varied.

Imipramine was given in standard but flexible doses, starting with 25 mg. 3 times daily; if there was only transient or no response, 50 mg. thrice daily was then given. One-third of the patients (33) failed to recover on this regimen and were given 75 or 100 mg. 3 times daily, which was the highest dose used. Because of the danger of relapse the optimum dose was continued for at least 8 weeks after its maximum effect and was then slowly reduced. Concomitant E.C.T. was necessary in 12 patients. Response to treatment was graded on a 5-point scale, from "complete recovery" to "worse", using explicit clinical criteria. All the patients were followed up for 3 to 6 months.

Of the 100 patients, 59 recovered and 20 were much improved; a further 9 were rated as improved, 8 showed no change, and 4 were worse. Taken by types of depression, 41 of the 48 manic-depressives and all 22 patients with endogenous illness recovered or were much improved. On the other hand, the 10 psychoneurotics responded comparatively poorly: none recovered, one got worse, and 4 showed no change. Considering patients from the other viewpoints mentioned above, 18

were thought unfit for E.C.T.; of these, 13 recovered, 3 were much improved, and 2 improved. There were 29 patients who had responded inadequately to E.C.T. (and this included 12 who had been in hospital for more than a year); of these, 2 recovered and 6 were much improved. Of the group of 26 patients previously treated with E.C.T., 22 were manic-depressives; 16 of these recovered and 4 were much improved. Finally, of the 27 patients with a first attack of depression, 18 recovered and 6 were much improved. A number of patients (64, including at least 9 of those unfit for E.C.T.) acted as their own controls.

Considered over-all, the symptoms of the depressive syndrome improved as an entity and not separately. Optimum dosage and rate of response appeared to be idiosyncratic. Atropine-like side-effects included dryness of the mouth, which always passed off within several days; shakiness and agitation, requiring additional treatment in 6 cases and withdrawal of the drug in 3 others; and dizziness, which cleared spontaneously in 6 of 7 cases. Epileptic fits occurred in 3 elderly patients while they were taking the drug, but they did not persist. Purpura simplex occurred twice, and there was one case of granulocytosis; in none could imipramine be directly implicated, as the patients were also receiving other drugs at the time. No other significant change in blood count or in liver dysfunction was seen.

[These results are consistent with, and slightly better than, those reported by other workers. Although further investigation and comparison with other antidepressants are needed, the position and potential value of imipramine are favourably compared with those of chlorpromazine (to which it has a structural similarity) in the treatment of schizophrenia.] *Alan A. Black*

561. **Factors Related to the Outcome of Depression Treated with E.C.T.**

M. HAMILTON and J. M. WHITE. *Journal of Mental Science* [*J. ment. Sci.*] **106**, 1031–1041, July [received Oct.], 1960. 6 refs.

A group of 49 out of 68 males admitted consecutively to the Stanley Royd Hospital, Wakefield, with severe depressive illness have been investigated to determine the factors related to outcome after treatment with electric convulsion therapy (E.C.T.). Their mean age was 51·7 years (range 21 to 69 years, but with two-thirds above 50 years), and the length of illness extended from one to 10 months, except for 9 patients whose illness had lasted up to 10 years. Independent assessments were made of 17 depressive symptoms in each patient, and the sum of these was taken as the patient's "depressive score". The usual course of E.C.T. consisted of 6 treatments (minimum 4, maximum 10). In 14 patients the course had to be repeated because of a rapid return of symptoms. Each patient's depressive score was again assessed at least one month after the end of treatment.

The depressive illnesses were classified as "endogenous", "doubtful endogenous", "doubtful reactive", and "reactive". The mean initial depressive score diminished in that order. The worst therapeutic results occurred in the "doubtful endogenous" category, which had clinically the same symptoms as the "endogenous" category, from which it was distinguished merely by the presence of minor psychological stress in the aetiology. Good prognostic signs were (*a*) absence of paranoid symptoms; (*b*) pyknic physique; (*c*) great initial weight; (*d*) initiation of treatment at the third or fourth month of illness; and (*e*) a measurable fall in blood pressure in the Funkenstein (mecholyl) test. Of no prognostic significance were: (*a*) age; (*b*) history of mental illness in the family; (*c*) previous neurotic traits; (*d*) physical or psychological precipitation of the illness; (*e*) sudden or gradual onset; (*f*) steady or fluctuating course; and (*g*) number of previous attacks. *F. K. Taylor*

562. **A Controlled Trial of Iproniazid in the Treatment of Endogenous Depression**

L. G. KILOH, J. P. CHILD, and G. LATNER. *Journal of Mental Science* [*J. ment. Sci.*] **106**, 1139–1144, July [received Oct.], 1960. 12 refs.

In a study at the Newcastle General Hospital and St. Nicholas' Hospital, Newcastle upon Tyne, 81 in-patients suffering from endogenous or involutional depression were allocated in turn to one of 3 treatments: iproniazid, placebo, or electric convulsion therapy (E.C.T.). Doubtful cases were excluded, as were patients whose condition did not warrant the risk of 3 weeks' ineffective treatment. Iproniazid, 50 mg. 3 times daily, and placebo tablets were given for a minimum of 3 weeks. If there was inadequate improvement after this time E.C.T. was given. Each patient assigned to the E.C.T. group had the optimal number of shocks for his condition. Clinical assessment was made weekly. In patients given tablets who showed no improvement, final assessment was made after 3 weeks. When significant improvement occurred, this was usually evident after 3 to 4 weeks, and it was never necessary to delay final assessment later than 6 weeks. In the E.C.T. group final assessment was made 7 to 10 days after the last treatment.

The patient's condition was rated as worse, unchanged, slightly improved, greatly improved, or symptom-free. The first three categories were combined as a poor result, and the last two constituted a good result. A good result was obtained in 14 of the 26 patients receiving iproniazid, compared with 24 out of 27 patients given E.C.T. and 3 of 28 patients the placebo. Side-effects were trivial and never necessitated withdrawing the iproniazid. Neither jaundice nor peripheral neuritis was seen in this series.

It is concluded that iproniazid is effective in the treatment of depression, but not as efficacious as E.C.T., considering immediate results. However, as relapses occur most frequently 3 to 6 months after E.C.T., comparison of results of iproniazid at that time is perhaps more important. Such a follow-up study will be reported later. *Alan A. Black*

563. **Comparative Clinical Experience with Five Antidepressants**

J. P. HOLT, E. R. WRIGHT, and A. O. HECKER. *American Journal of Psychiatry* [*Amer. J. Psychiat.*] **117**, 533–538, Dec., 1960. 3 refs.

Dermatology

564. **The Action of ACTH, Cortisone and Prednisone on the Connective Tissue of Normal and Sclerodermic Human Skin**

R. E. MANCINI, S. G. STRINGA, and L. CANEPA. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **34**, 393–417, June, 1960. 36 figs., 23 refs.

At the Facultad de Ciencias Medicas, Buenos Aires, Argentina, the authors have studied the action of ACTH (corticotrophin), cortisone, and prednisone on human skin. For this they used skin from 6 healthy volunteers, and from 30 patients with local diseases capable of temporary improvement by hormone therapy. The three hormones were administered parenterally and by mouth, and hydrocortisone ointment was applied locally.

The results obtained in both normal and diseased skin were constant. Normal skin showed progressive atrophy of the collagen bundles and fibres, thinning and fragmentation of the reticular and elastic fibres, and disappearance of the interfibrillar mucopolysaccharides. The basement membrane appeared to become thin and lose its continuity, while the periodic-acid–Schiff reaction became weaker. Fibroblasts lost nucleoprotein granules from their cytoplasm and the nuclei were pyknotic. In scleroderma and scleroedema adultorum the hypertrophied collagen bundles and the elastic tissues became dissociated, the zones of hyalinization became reduced, and the mucopolysaccharide in the papillary corium disappeared. The glycoprotein, the reticular fibres of the basal membrane, and the hyalinized arterioles were unchanged. Fibroblasts seemed less hypertrophied and lost their cytoplasmic nucleoproteins. Some mast cells lost their granules. All the changes described reached their peak about 4 weeks after treatment, and appeared more marked with prednisone than with corticotrophin or cortisone. The changes were apparently reversible, since the skin returned to normal when administration of the hormones ceased.

[This paper is illustrated with extremely clear plates.]

G. B. Mitchell-Heggs

565. **Toxic-allergic Reactions Associated with Chlorpromazine Treatment.** (О некоторых токсико-аллергических реакциях, связанных с применением аминазина)

A. B. SMULEVIČ. *Журнал Невропатологии и Психиатрии* [*Ž. Nevropat. Psihiat.*] **60**, 585–592, No. 5, 1960. 1 fig., 43 refs.

Out of 1,000 schizophrenic patients treated with "aminazine" (chlorpromazine) 90 developed dermatitis. This complication showed some relation to seasonal variation, 44 of the cases occurring in spring, 11 in summer, 12 in autumn, and 23 in winter. This variation, it is suggested, may be due to vitamin deficiencies in the winter months. [Kalamaryan, however, in another paper in the same journal, reports that such patients showed hypersensitivity to sunlight.]

The dermatitis was of a bullous form, with subsequent necrosis of the dermis, in 8 cases, of which 4 occurred after repeated courses of treatment with aminazine, but were mild and subsided on withdrawal of the drug. In the other 4 cases, however (all in women), the reaction was severe, appeared soon after administration of aminazine, and in spite of withdrawal of the drug progressed to a fatal issue. In all 4 of these severe cases there was a history of rheumatism with recurrences, or of repeated attacks of tonsillitis, and 3 of the patients were near the menopause. Two had previously received courses of aminazine, and one had developed hepatitis after treatment with "achrichin" (mepacrine). The first symptom was pyrexia, followed by formation of bullae on the buttocks, waist, neck, and soles of the feet. The skin was greyish white, the lips cyanosed, while other signs and symptoms were sweating, dyspnoea, tachycardia, pain in the joints, aphthous stomatitis, and hepatomegaly. There was a moderate leucocytosis, with eosinopenia, a raised erythrocyte sedimentation rate, and a progressive fall in the blood pressure. In the severe cases the patients all died of peripheral heart failure.

The dosage of aminazine was 100 to 300 mg. per day, which is a normal therapeutic dose. It is urged therefore that in the treatment of patients with a previous history of rheumatism, drug allergy, recurrent tonsillitis or other infections this drug should be used with extreme caution. [See also Abstract 566.]

L. Firman-Edwards

566. **Morphological Changes in the Bullous-necrotic Form of Chlorpromazine Toxic Dermatitis.** (Морфологические изменения при буллезно-некротической фозме аминазиновой токсикодермин)

A. P. LEVKOVIČ-SOKOLOVA. *Журнал Невропатологии и Психиатрии* [*Ž. Nevropat. Psihiat.*] **60**, 595–601, No. 5, 1960. 6 figs., 7 refs.

The author describes the post-mortem findings in the 4 fatal cases of dermatitis following treatment with chlorpromazine reported above [see Abstract 565]. In addition to the skin lesions, which included formation of bullae, desquamation, and necrosis, focal haemorrhages were found in the mucosa of the large bowel in one case, and in all 4 cases there was oedema of the meninges, dilatation of the cerebral ventricles, subarachnoid cysts, focal softening of the brain substance, accompanied by oedema, dystrophic myocardial changes, acute renal glomerulitis with tubular dystrophic changes, and serous hepatitis with, in one case, moderate hepatic cirrhosis. In many parts of the body the arteries showed plasma infiltration of the media, fibrinoid necrosis of the intima and adventitia, and perivascular oedema and haemorrhage.

The author considers that in these cases there is, in addition to the allergic factor, a trophic effect of the toxaemia of the central nervous system, and sees a resemblance between the skin lesions found in the present cases and the acute bedsores which occur in cases of coal-gas poisoning and sometimes in post-encephalitic Parkinsonism. He points out that all 4 patients were women near the menopause, and suggests that hormonal imbalance may play a part in the pathogenesis.

L. Firman-Edwards

567. **Plant Dermatitis**

A. ROOK. *British Medical Journal* [*Brit. med. J.*] **2**, 1771–1774, Dec. 17, 1960. 31 refs.

568. **Treatment of Chronic Furunculosis**

L. G. TULLOCH, V. G. ALDER, and W. A. GILLESPIE. *British Medical Journal* [*Brit. med. J.*] **2**, 354–356, July 30, 1960. 15 refs.

The authors of this paper from the United Bristol Hospitals describe the treatment of 58 adult patients suffering from recurrent furunculosis of at least 6 months' duration. Alternate patients were placed in either a treatment group or a control group and from all the patients swabs were taken at monthly intervals from a furuncle, the anterior nares, the ears and eyelids, and later in the trial from the perineum; swabs were also taken from the relatives of some of the patients. In both groups of patients the boil-bearing areas were swabbed with a 1 in 3,000 solution of mercuric chloride twice a day.

The treatment group, but not the controls, were given an antiseptic cream, usually consisting of a combination of neomycin and bacitracin, to apply to the anterior nares 2 or 3 times daily for 3 months. The same cream was also applied to the eyelids of those patients in whom culture of the eye swabs was positive in the absence of any clinical evidence of inflammation; if obvious blepharitis was present a cream containing hydrocortisone and neomycin was used. Ear-drops with these active ingredients were used in the treatment of otitis externa, while a hexachlorophane bath or a talcum powder containing 3% hexachlorophane was prescribed for patients in whom cultures of perineal swabs were positive.

In all, 33 patients in the treated group and 23 controls were followed up for 4 to 6 months. Of the controls 3 were cured and 20 continued to have boils; of the treated group 22 remained free from lesions, one improved, and 5 were unchanged. In the remaining 5 cases family sources of re-infection had to be eradicated before cure was effected. Cultures taken from the anterior nares remained positive in 5 out of 24 patients in the treated group and in 17 out of 20 controls. Nasal swabs were taken from 22 families, and from 14, strains which were similar to those in the patients were isolated from one or more relatives. All except 7 of the 58 patients were nasal carriers of the strains which caused the boils.

The authors emphasize the importance of obtaining the patients' co-operation in the successful treatment of the staphylococcal carrier state. *P. T. Main*

569. **Curettage and Electrodesiccation in the Treatment of Skin Cancer**

J. M. KNOX, T. W. LYLES, E. M. SHAPIRO, and R. D. MARTIN. *Archives of Dermatology* [*Arch. Derm.*] **82**, 197–204, Aug., 1960. 5 figs., 14 refs.

It is pointed out that although curettage followed by electrodesiccation is probably the most-widely used method of treating cancer of the skin, it has received little attention in the literature. The records of all patients with cancer of the skin treated in this way at Jefferson Davis Hospital, Houston, between January, 1939, and January, 1959, were reviewed. Of 441 patients in whom epitheliomata were histopathologically diagnosed 345 subjected to curettage and electrodesiccation were followed-up for a minimum of 6 months. Altogether there were 765 lesions (315 squamous-celled and 450 basal-celled epitheliomata).

Of 90 lesions in 67 patients followed up for more than 5 years 3 recurred, giving a cure rate of 96·7%, and of the total of 765 lesions 13 recurred, giving a composite overall cure rate of 98·3%. All the recurrences responded to further similar treatment and there were no metastases. None of the patients died.

In the authors' view curettage and electrodesiccation of cancerous skin lesions results in a cure rate which compares favourably with that of other methods. The disadvantages are that the method is not appropriate for large and invasive lesions, treated sites heal more slowly than with excision, and hypertrophic scars may develop. However, in general, cosmetic results are usually good.

Benjamin Schwartz

570. **Treatment of the Dermatoses with 6-Methylprednisolone.** (Über Erfahrungen mit 6-Methyl-Prednisolon bei Dermatosen)

W. KNOTH and B. GÖBEL. *Dermatologische Wochenschrift* [*Derm. Wschr.*] **142**, 801–804, July 16, 1960. 35 refs.

From the University Skin Clinic, Giessen, Germany, comes this report on the efficacy of treatment with 6-methylprednisone of 62 patients, most of whom were suffering from such conditions as eczema, psoriasis, dermatomycosis, and urticaria, while a few had primarily dermal diseases such as systemic lupus erythematosus and sarcoidosis. The duration of therapy ranged from 10 to 74 days (average 23 days) and the total dose of the steroid from 80 to 2,384 mg., the dosage depending largely upon the type and severity of the disease in each case. Investigations carried out before and during therapy included determination of blood pressure and blood sugar, serum protein, and electrolyte levels. There appeared to be no major alterations in any of these values as a result of the therapeutic regimen, except that the serum potassium level was lowered in 18 cases. However, only one patient, in whom this level was 13·6 mg. per 100 ml., developed symptoms. There was a general increase in the feeling of well-being and no important complications occurred. The dosage of methylprednisone was between 50% and 75% of that of prednisolone, while it was considered that the former was more easily utilized. The importance of supplementary potassium therapy is emphasized. *Allene Scott*

Paediatrics

571. **Blood Loss in Paediatric Surgery**
J. A. PRETORIUS. *Anaesthesia* [*Anaesthesia*] **15**, 424–432, Oct., 1960. 2 figs., 9 refs.

A study of gravimetric blood loss estimations is presented in a series of 443 paediatric surgical operations. It is established that the operations for Thiersch graft to burns, incision and drainage of acute osteomyelitis and major urological surgery involve considerable blood loss. The former two divisions present the greatest danger in that the precipitous nature of the loss is often not anticipated. The importance of a poor nutritional state, relative to the stress of the presenting illness, anaesthesia and surgery is emphasized. There exists a need for more extensive investigation into blood loss during paediatric ENT surgery.

A simple practical gravimetric method of blood loss estimation during paediatric surgery is presented. Although admittedly not ideal it has served to eliminate the fallacious guessing commonly termed "clinical estimation of blood loss".—[Author's summary.]

INFANT FEEDING

572. **Evaluation of Infants Fed Soybean and Evaporated Milk Formulae from Birth to Three Months: a Comparison of Weight, Length, Hemoglobin, Hematocrit, and Plasma Biochemical Values**
J. L. KAY, C. W. DAESCHNER JR., and M. M. DESMOND. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **100**, 264–276, Aug., 1960. 10 figs., 38 refs.

The total weight and length gains of normal infants receiving soybean milk and evaporated milk formulae were similar, as were the patterns of weight and length increase. The individual growth curves of infants fed soybean formula and evaporated milk formula are presented on Iowa Growth Charts [Jackson *et al.*, "Growth Charts for Use in Pediatric Practice", *J. Pediat.*, 1945, **27**, 215], and the weight and length increase of these two study groups of patients are also presented in graph form. Physical examinations and developmental achievements of these patients were similar.

Hemoglobin and hematocrit values were comparable in infants fed a soybean milk formula, infants fed an evaporated milk formula, and control infants on *ad libitum* diets. These values were considered normal. The values for hemoglobins and hematocrits at 3 months were also similar to each other and to those reported by others. Plasma biochemical determinations at birth and again at 3 months of age revealed comparable values for all three study groups. Total plasma cholesterol increased significantly by the age of 3 months in infants fed *ad libitum* diets, but not in infants fed soybean milk. The total serum protein and the partition of the protein fractions by paper electrophoresis were carried out at birth and at 3 months. These determinations showed no significant difference in the three groups except for a marked fall in the level of γ-globulin in all patients at 3 months of age.—[Authors' summary.]

573. **Absorption, Excretion, and Retention of Strontium by Breast-fed and Bottle-fed Babies**
E. M. WIDDOWSON, J. E. SLATER, G. E. HARRISON, and A. SUTTON. *Lancet* [*Lancet*] **2**, 941–944, Oct. 29, 1960. 19 refs.

To ascertain the strontium turnover in young babies, 9 breast-fed and 9 bottle-fed babies of similar birth weight were studied on the 6th, 7th, and 8th days after birth. The study, which took place at the Maternity Hospital, Cambridge, was confined to the stable element because of low levels of the isotope ^{90}Sr in the excreta of the babies during the period of investigation. Accurate test weighing was carried out on the breast-fed babies to ensure how much milk was taken. Each mother's milk was analysed for strontium content, as were samples from 15 other breast-feeding mothers. The bottle-fed babies were given a mixture of dried whole cow's milk and lactose specially prepared for the investigation, but when the strontium content was found to be half that of the commercial dried milk in current use in the hospital, 6 of the infants were given the special preparation and 3 the standard commercial milk. All the urine, faeces, and regurgitated food were collected during the 3-day study period and analysed for strontium, calcium, and phosphorus. The milk given was similarly analysed.

The strontium content of the special dried cow's milk preparation was about 4 times, and of the standard commercial preparation 8 times, that of the breast-milk samples. The amounts of calcium and phosphorus in the two cow's-milk preparations were identical, and 4 times (calcium) and 5 times (phosphorus) as high as in the breast milk. The average strontium intake of the bottle-fed babies was 4 and 8 times as high as of those who were breast-fed, yet the breast-fed babies excreted about 7 times as much strontium in the urine. These breast-fed babies excreted as much strontium in the urine as in the faeces, each of which contained more strontium than the food. They were thus in strongly negative strontium balance, though they were in positive balance for such dietary constituents as calcium and phosphorus. The bottle-fed babies were in positive strontium balance, excreting most of the strontium by the bowel, the urinary excretion amounting to only 7 to 10% of the total, in contrast to 50% in the breast-fed babies.

The infants fed on the commercial milk, which contained more strontium, retained 5 times as much strontium as those on the specially prepared milk, but their faecal excretion was no higher. When the metabolism

of strontium was considered together with the absorption and excretion of calcium and phosphorus it appeared that the body discriminates against strontium in favour of calcium at different ages. Both commercial milks contained much less strontium in relation to calcium than the adult diet, showing that calcium is preferentially secreted in milk. Pursuing the possibility that the low content of phosphorus in breast milk might account for the elimination of strontium from the bones of breast-fed babies and for the higher urinary excretion of strontium than in bottle-fed babies, 8 breast-fed babies were given 120 mg. of phosphorus daily on the 5th, 6th, and 7th days after birth. The urine passed on the 7th full day after birth contained less strontium than that of any of the babies on breast milk alone, the average excretion of strontium being nearly as low as in the bottle-fed babies. The urinary calcium was also reduced, indicating that calcium and strontium respond to additional phosphorus in the same way. *David Morris*

574. **Hypersensitivity to Milk and Sudden Death in Infancy**

W. E. Parish, A. M. Barrett, R. R. A. Coombs, M. Gunther, and F. E. Camps. *Lancet* [*Lancet*] **2**, 1106–1110, Nov. 19, 1960. 5 figs., 10 refs.

Sudden death in infancy has been a subject of considerable speculation and investigation by clinicians and pathologists. The hypothesis that it may be due to an anaphylactic type of reaction from the inhalation of cow's-milk protein regurgitated during sleep is strongly supported by experimental work carried out on guinea-pigs as described in this paper from the University of Cambridge. The majority of infants fed on cow's milk develop antibodies to milk protein, and in 286 normal infants the average titre was around 64. In 24 " cot-death " cases the antibody titre was suggestively higher, particularly when allowing for the delay in collecting blood after death. Previous work had shown that a small amount of cow's milk dropped into the larynx of sensitized guinea-pigs resulted in a characteristic anaphylactic reaction which often led to death. The stomach contents from 4 " cot-death " cases were introduced into the larynx of lightly anaesthetized sensitized and unsensitized control guinea-pigs. Almost all the sensitized guinea-pigs died " silently, without any struggle, and in a very short time ", while among the control animals there were no deaths or even clinical effects. When the antibody response in guinea-pigs to the individual constituents of cow's milk was analysed, casein and β-lactoglobulin proved equally antigenic and in sensitized guinea-pigs equally lethal, while α-lactalbumin was only mildly antigenic and relatively innocuous. The pathological findings in the lungs of sensitized guinea-pigs which died after the inhalation of reconstituted dried milk, casein, or β-lactoglobulin were similar to those in animals which died after the experimental introduction of stomach contents from "cot-death" cases, that is, generalized congestion with only an occasional small area of oedema and little cellular infiltration, chiefly of macrophages. The histopathological findings were not unlike those in the " cot-death " cases.

[This is an important and original paper which, if supported by further experimental work, may prove of considerable significance to those investigating the relatively large number of infants found dead each year in their cots.] *David Morris*

NEONATAL DISORDERS

575. **Acquisition of Staphylococci by Newborns. Direct versus Indirect Transmission**

E. Wolinsky, P. J. Lipsitz, E. A. Mortimer Jr., and C. H. Rammelkamp Jr. *Lancet* [*Lancet*] **2**, 620–622, Sept. 17, 1960. 1 fig.

The work here reported from the Cleveland (Ohio) Metropolitan General Hospital forms the first part of a wider study of the important modes of transmission of neonatal infections. It was designed primarily to determine whether infant-to-infant spread was direct (heavy droplets projected short distances) or indirect (airborne droplet nuclei or dust). A special nursery was devised in which was placed an " index " infant, known to be a nasal carrier of a phage-typable strain of staphylococcus. A different index infant was used each week. Six newborn infants at a time were exposed to an index infant at fixed but different distances. The 6 newborn infants were cared for by a staff of the same 3 nurses working in shifts. These nurses did not touch the index infant, whose needs were attended to by personnel summoned from outside the nursery.

Of 48 infants exposed, only one appeared to have an organism identical with that of the index infant. In contrast to this low rate of spread from infant to infant there was a high rate of acquisition of organisms of phage types identical with those isolated from 2 of the 3 nurses. It thus appears that spread of organisms from staff to infant is more important in the dissemination of infection than is spread from infant to infant.

Winston Turner

576. **Sudden and Unexpected Death in Early Life**

S. S. Morrison. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **173**, 1199–1204, July 16, 1960. 5 figs., 19 refs.

Reduction in the incidence of sudden death in infants and children depends on prompter recognition of significant symptoms and signs which have preceded such an event. With this in mind the author has reviewed the cases of sudden death in this age group which have occurred over a 6½-year period at the Geisinger Memorial Hospital, Danville, Pennsylvania. During this time 189 paediatric deaths were recorded, and 17 (9%) of these were classified as unexpected. Ages ranged from 1 day to 30 months, and symptoms had not been present for more than 48 hours in any instance. Investigations included examination of cultures of the heart blood made within 10 minutes of death, of nose and throat cultures, and of anal-swab cultures; the cerebrospinal fluid was also examined. Necropsy findings supported Boyd's opposition to the concept of status thymicolymphaticus, the thymic weight in the first year of life ranging

from 4·4 to 38 g. There was no case of mechanical suffocation, and only one case of congenital anomaly (heart malformation) with death on the first postnatal day. Unexpected death in the course of known disease under treatment occurred twice (nephrotic syndrome treated with corticotrophin; birth injury). In 11 cases symptoms began within 48 hours of death in previously healthy babies. Infection was demonstrated in 7 cases (septicaemia 4, meningitis 2, croup 1), and there were 3 cases of endocardial fibroelastosis. Of the 4 infants found dead in their cots, one had a minor illness of 48 hours' duration, but 3 had appeared normal and well. Pulmonary oedema was present in all 4 cases, but the author questions the significance of this finding. A reduced γ-globulin level was found in the infant with a minor infection, and it is suggested that this might have been an important factor in the fatal outcome.

A. White Franklin

CLINICAL PAEDIATRICS

577. **Congenital Biliary Atresia**

R. CAMERON and G. L. BUNTON. *British Medical Journal* [*Brit. med. J.*] **2**, 1253–1257, Oct. 29, 1960. 5 figs., 17 refs.

In this report from University College Hospital, London, the authors discuss the embryological, pathological, and clinical features of congenital biliary atresia. In one of their 4 patients surgical treatment was successful, and they were able to study the histology of the liver at a later date. They comment on the disappointing rarity of successfully treated cases of this abnormality, and briefly describe the 3 unsuccessful cases. In the fourth patient liver biopsy and choledocho-duodenostomy were performed at 2 months of age, and the child was perfectly well at 4 years, when a second liver biopsy was carried out. A detailed description is given of the two biopsy specimens; the first showed the typical features of major duct obstruction in infancy, and the second only minimal departures from a normal pattern. The authors comment on the lack of information in the literature regarding the histological recovery of the human liver following relief of prolonged biliary obstruction, but refer to experimental studies in animals in which release of extrahepatic duct obstruction was followed by the conversion of quite marked degrees of biliary cirrhosis to a normal histological pattern.

The embryology of the liver and bile-ducts is described, and it is suggested that, though many cases of atresia might be accounted for by aberrations in development, not all are easily explained in this way. The diagnosis of the condition is briefly discussed. Operation after a short period of investigation and observation, possibly including a trial of dehydrocholic acid in an attempt to clear blockage of anatomically patent ducts, is advocated. The authors suggest that at laparotomy a complete dissection of the extrahepatic ducts should be made, combined with the injection of saline solution, and cholangiography performed if appropriate.

[The most important point in this paper is the histological evidence of restoration of normal liver architecture following relief of obstruction. Those interested should refer to subsequent correspondence (*Brit. med. J.*, 1960, **2**, 1959), in which certain controversial statements are discussed.] *E. G. Hall*

578. **Possibility of Iatrogenic Factors Responsible for Hypernatremia in Dehydrated Infants**

V. R. DEYOUNG and E. F. DIAMOND. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **173**, 1806–1808, Aug. 20, 1960. 16 refs.

It is pointed out that over the past 10 years there has been a marked increase in the incidence of hypernatraemia in dehydrated infants, with all its sequelae of neurological complications. In this paper a study is reported of 47 patients, under 4 years of age, who were admitted to hospital with acute diarrhoeal disease over the 2-year period 1957–9. Of these 47 patients 10 had hypernatraemia with a serum sodium concentration of 150 mEq. per litre or higher, and in 3 of these, who were only moderately ill on admission, the condition deteriorated markedly, with signs of central nervous system involvement, following parenteral saline therapy. A further 6 patients who were severely ill on admission had been given milk and other electrolyte-containing fluids at home. In 3 of the patients in the series there were neurological sequelae—namely, convulsions and slowed mental development over the next few years. There were 2 deaths, a mortality of 20%.

It has been postulated that the damage results from the administration of relatively large quantities of electrolytes (chiefly salt), because of failure to realize that infants lose relatively large quantities of water and not much salt during diarrhoeal episodes. The sodium causes vascular damage, which is not revealed initially since that cation reduces vascular permeability. As soon as dilution occurs as a result of therapy, however, there is a rapid exodus of fluid and blood from the vessels, with the production of meningeal haemorrhage and subdural haematoma. Necropsy in one of the fatal cases in this series revealed a subdural effusion; the brain in the other case was not examined. *Allene Scott*

579. **Faecal Incontinence in Children: The Physical Factor**

M. COEKIN and D. GAIRDNER. *British Medical Journal* [*Brit. med. J.*] **2**, 1175–1180, Oct. 22, 1960. 4 figs., 10 refs.

Until 1948 the causes of colonic dysfunction in children were inadequately differentiated. In that year the work of Swenson and Bill (*Surgery*, 1948, **24**, 212; *Abstr. Wld Surg. Obstet. Gynaec.*, 1949, **5**, 340) led to Hirschsprung's disease being defined as an obstruction due to an aganglionic segment of bowel. This left the way open for the study of non-obstructive forms of megacolon in children, and two schools of thought have arisen as to the faecal incontinence which often accompanies the constipation, one supporting a mechanical basis and the other an emotional one. Against this background the present authors have studied all children presenting with faecal incontinence at Addenbrooke's Hospital, Cambridge, since 1949, in an attempt to arrive at some con-

clusion regarding aetiology, and they now present an analysis of the 69 cases treated during the 11 years up to 1959. Children with severe mental retardation, ectopic or stenosed anus, or meningomyelocele were excluded. During the 11 years only 6 cases of true Hirschsprung's disease were seen. According to the authors the differentiation can usually be made on clinical grounds, but in the neonatal period radiological investigation may be necessary.

Most of the 69 children fell into one of the 2 main groups mentioned above. In the larger group of 44 cases the soiling had a mechanical basis, with constipation as the primary condition and the soiling due to overflow incontinence, semi-liquid matter having leaked past hard, impacted faecal masses. This condition is described as colonic inertia; it usually began in the first 4 years of life, and sometimes in the first few months, and responded to vigorous treatment of the constipation by aperients, diet alone being inadequate. Psychological disturbances in this group were secondary, often surprisingly slight, and disappeared with the successful treatment of the primary condition.

In the second group, of 15 cases, the incontinence was judged to be psychogenic. Here onset was later than in the first group, with boys more often affected than girls, and there was generally no constipation, the stools being, at least initially, of normal consistency. Nearly all these children displayed other signs of emotional disturbance in addition to the faecal incontinence. The authors term this condition encopresis (Weissenberg's analogue to enuresis) and consider that it must be treated primarily by psychiatric means.

In the remaining 10 cases somatic and psychic factors were so interwoven that neither could be considered to be the primary influence. *Marianna Clark*

580 (a). **Iron Deficiency in the Premature Infant. Significance, and Prevention by the Intramuscular Administration of Iron-dextran**

J. A. JAMES and M. COMBES. *Pediatrics* [*Pediatrics*] **26**, 368–374, Sept., 1960. 1 fig., 33 refs.

580 (b). **Comparison of Oral and Intramuscular Administration of Iron for Prevention of the Late Anemia of Premature Infants**

A. L. SITARZ, J. A. WOLFF, and F. H. VON HOFE. *Pediatrics* [*Pediatrics*] **26**, 375–386, Sept., 1960. 11 refs.

These two papers seek to demonstrate that intramuscular administration of iron is effective in preventing anaemia in premature infants. In the study described in the first paper, from Parkland Memorial Hospital, Dallas, Texas, 205 consecutive prematurely born infants, weighing 2,000 g. or less at birth and surviving at least 24 hours were allocated by random selection to a group to receive iron–dextran (" imferon ") or to a control group. A total of 181 infants survived the neonatal period and on reaching a weight of 2,000 g. 84 were given 1 ml. of iron–dextran (50 mg. of elemental iron) daily for 5 days and 97 served as controls. The diet in both groups of infants was the same. Duplicate haemoglobin (Hb) and microhaematocrit values were determined weekly in the nursery and monthly at follow-up visits.

In the treated infants the Hb level was significantly higher at the age of 9 to 10 weeks than in controls. The mean Hb level at 24 weeks was 12·2 g. per 100 ml. in the treated group and 8·8 g. per 100 ml. in the controls. Only 5 controls reaching the age of one year had a Hb level above 9·5 g. per 100 ml. There was no significant difference between the two groups in respect of weight or general development, or the incidence of infections as indicated by in-patient and out-patient attendances. The authors suggest that although iron by mouth is effective when given regularly and under supervision, prophylactic injection is more likely to succeed in an indigent population.

In the second paper, from the Babies Hospital, New York, a study is reported of 100 premature babies weighing less than 1,800 g. at birth, who were given either a ferrous sulphate preparation by mouth in a dosage of 0·6 ml. daily until the age of 2 to 3 months when it was doubled or a calculated dose of iron–dextran intramuscularly from the time they weighed 2,100 g. Of the 80 remaining in the study 37 received the oral preparation and 43 received intramuscular injections. For purposes of evaluation the infants were divided into groups according to birth weight: (1) less than 1,200 g., 18 infants; (2) 1,200 to 1,499 g., 23 infants; and (3) 1,500 to 1,799 g., 39 infants, the haemoglobin level, erythrocyte count, reticulocyte count, and erythrocyte indices in infants given iron by mouth and those given iron intramuscularly in the different groups being then compared. The authors conclude that iron intramuscularly is as effective as iron by mouth in the " treatment of the late anemia of prematurity ", although they prefer the latter when regular administration is assured.

The results of this investigation were compared with those obtained in 1954 in a group of untreated infants of comparable weight from the same nursery. The haemoglobin levels in infants given iron by mouth irregularly compared favourably with those in infants given the prescribed dosage by mouth or the intramuscular injections, suggesting that the amount of iron prescribed for oral administration in the present study was greater than that actually required.

An addendum to each of these papers notes that the preparation of iron–dextran used (imferon) has been withdrawn, at least temporarily, because of toxicity in animals. *A. White Franklin*

581. **Postoperative Care and Complications after Tracheotomy in Infants and Children.** [In English]

N. G. TOREMALM. *Acta anaesthesiologica Scandinavica* [*Acta anaesth. scand.*] **4**, 105–124, 1960. 11 figs., 27 refs.

A continuous uniform post-tracheotomy care adopted in a hospital [University Hospital of Lund, Sweden] with more than 200 tracheotomies annually is described. No noteworthy complications were seen in 25 consecutive cases of children under 10 years of age. The results are compared with earlier statistics, and prophylactic steps are discussed.

Heat and moisture exchangers for connection with the tracheal cannula have been constructed and tested both experimentally and clinically. They are able to treble

the absolute humidity of inspired room air, and good clinical results were obtained, even in cases where ordinary steam therapy proved ineffective. The dead spaces and air-flow resistances of the apparatuses are made equal to that of the upper respiratory tract, which seems to be an additional improvement, facilitating normal respiration after decannulation.—[Author's summary.]

582. **Measurement of Respiratory Effort and Assessment of a Method of Treating Lower-respiratory-tract Infections in Small Children**

W. W. HOLLAND, J. R. T. COLLEY, and M. A. BARRACLOUGH. *Lancet* [*Lancet*] **2**, 1166–1167, Nov. 26, 1960. 1 fig., 3 refs.

Intraoesophageal pressures and trunk expansion were measured in 11 children with lower-respiratory-tract infections before and after injection of adrenaline. The product of intraoesophageal-pressure swing and respiratory rate was taken as a measure of respiratory " effort ". Those children with airway obstruction showed considerable reduction in respiratory " effort " after adrenaline. —[Authors' summary.]

583. **Association of the Chimpanzee Coryza Agent with Acute Respiratory Disease in Children**

M. BEEM, F. H. WRIGHT, D. HAMRE, R. EGERER, and M. OEHME. *New England Journal of Medicine* [*New Engl. J. Med.*] **263**, 523–530, Sept. 15, 1960. 8 refs.

In this paper from Bobs Roberts Memorial Hospital for Children, Chicago, the authors report the isolation of a virus antigenically similar to the chimpanzee coryza virus from a group of children suffering from acute respiratory infection.

Between December, 1958, and June, 1959, they studied 125 in-patients and 166 out-patients, including affected children and controls; the former group contained 83 children admitted with acute respiratory infection (average age 1·6 years) and 42 controls (average age 5·8 years), while the latter group contained 80 children (average age 3·5 years) and 5 adults with acute respiratory illness and 81 child controls (average age 2·9 years). Pharyngo-nasal and rectal swabs were taken for virus culture and nose and throat swabs for bacteriological investigation. Paired sera were obtained where possible. The pharyngeal swabs were inoculated within 3 hours of collection into tissue culture tubes of H Ep-2 cells, then stored, together with the rectal swabs, at −30° C. The authors describe in detail their virological techniques, which included a search for haemadsorption viruses and entero- and adeno-viruses.

During the investigation 48 agents similar to the prototype virus (Randall) were isolated from 41 patients. The authors describe the characteristics of the virus in tissue culture, demonstrate its close antigenic relationship to the chimpanzee coryza virus, and emphasize its rapid loss of infectivity on storage at −30°C. All 41 patients from whom virus was isolated were suffering from acute respiratory infection, and 80% of the positive cultures were obtained during the first week of the illness. Isolation was most frequent in the youngest patients, cultures being positive in 21 of the 46 children under 6 months of age. Paired sera were available from 23 of the 41 culture-positive patients: in all 12 over 6 months of age, the complement-fixation or neutralization tests gave significant results, which, in the majority, were positive by both techniques; of the 11 infants under 6 months 4 gave a negative response by both methods. No cytopathogenic agent other than Randall virus was cultured from the positive swabs taken during the acute illness, and bacteriological investigations did not reveal any striking features.

Clinically, bronchiolitis, acute respiratory illness, and pneumonia were the most frequent conditions associated with isolation of Randall virus, cultures being positive for this virus in 17 out of 34 children (50%) with bronchiolitis and 8 out of 22 (36%) with pneumonia.

The authors conclude that a virus similar to the chimpanzee coryza agent can produce respiratory illness in human beings, that the infection is most severe in the infant, and that rapid inoculation of unfrozen material is desirable for satisfactory isolation of the virus.

E. G. Hall

584. **Acute Respiratory Infections in Children: Isolation of Coxsackie B Virus and Adenovirus during a Survey in a General Practice**

E. J. C. KENDALL, G. T. COOK, and D. M. STONE. *British Medical Journal* [*Brit. med. J.*] **2**, 1180–1184, Oct. 22, 1960. 1 fig., 17 refs.

The results are reported of virological and bacteriological examination of throat swabs from children with acute febrile respiratory infections seen in a general practice in the South of England between June, 1957, and December, 1958. The swabs were taken during the first 5 days of the illness. Of 702 acute respiratory illnesses in 595 children at risk 147 were investigated. In 41 (28%) of these one or more pathogens were isolated from throat swabs, Coxsackie viruses being isolated in 20. These illnesses occurred over a period of 12 weeks during the summer of 1958. Most of the patients had a febrile pharyngitis; moderately severe myalgia occurred in 2 cases and a transient meningeal reaction in one case. Adenoviruses (Types 1 to 4) were cultured in 4 illnesses characterized by pharyngitis, lymphadenopathy, and conjunctivitis. *Streptococcus pyogenes* was isolated from throat swabs in 18 illnesses, the pharyngitis in these being more severe than in other illnesses seen at the time.

No correlation was found between the clinical and the bacteriological and virological findings. *John Fry*

585. **Staphylococcal Empyema in Infants.** [In English]

K. BIE and J. STEEN. *Acta paediatrica* [*Acta paediat. (Uppsala)*] **49**, 605–608, Sept., 1960. 1 fig., 11 refs.

At Ullevål Hospital, Oslo, between September, 1957, and May, 1959, 8 infants (1 girl and 7 boys, aged 14 days to 23 months) were treated for staphylococcal empyema. All the infants were extremely ill on admission, but in none had the condition been diagnosed before they were admitted. All except 2 probably acquired the staphylococcal infection in a maternity hospital, where at that time there was a high incidence of such infections in mothers and infants (mastitis and

pyoderma). In all cases the clinical diagnosis was confirmed radiologically and by bacteriological examination of pus obtained by pleural puncture. Treatment with high doses of penicillin together with erythromycin or chloramphenicol was started on admission. In the first patient repeated pleural aspiration was carried out and in the remainder closed thoracotomy drainage, which was found to be preferable. Fibrinolytic enzymes were not used. All 8 patients recovered completely, the radiological appearances of the lungs being normal within 2 to 6 months. *Marianna Clark*

586. **Amino Acid and *alpha*-Keto Acid-induced Hyperinsulinism in the Leucine-sensitive Type of Infantile and Childhood Hypoglycemia**
M. M. GRUMBACH and S. L. KAPLAN. *Journal of Pediatrics* [*J. Pediat.*] **57**, 346–362, Sept., 1960. 13 figs., bibliography.

A study is reported of 2 male infants with the leucine-sensitive type of hypoglycaemia seen at the Babies Hospital, New York, when they were aged 15 months and 30 months respectively. Glucose-, adrenaline-, and glucagon-tolerance tests showed low fasting blood levels of glucose but a normally shaped curve. When L-leucine was administered by stomach tube in a dosage of 150 mg. per kg. body weight a rapid fall in blood glucose levels occurred within 15 minutes and the patients became semicomatose. No hypoglycaemic effects were observed with D-leucine, L-alanine, L-glycine, or DL-threonine. The effects of administration of the degradation products of leucine were then investigated; a sharp fall in the blood glucose level resulted from intravenous administration of sodium α-keto*iso*caproic acid, but no effect was observed with *iso*valeryl-coenzyme A or sodium α-keto-*iso*valerate. No excess accumulation of amino-acids in the blood or urine was observed throughout these investigations.

Further studies were undertaken to define the mechanism of hypoglycaemia, and the results suggest that L-leucine, L-isoleucine and α-keto*iso*caproic acid exert an insulin-like effect by stimulating insulin production from the islets of Langerhans, with a consequent rise in the plasma insulin level. *R. M. Todd*

587. **Chronic Endocrinopathies in Childhood.** [A Review]
W. A. REILLY. *Journal of Chronic Diseases* [*J. chron. Dis.*] **12**, 299–314, Sept., 1960. 10 refs.

588. **Studies on Thyroid Hormone Metabolism in Children**
H. M. HADDAD. *Journal of Pediatrics* [*J. Pediat.*] **57**, 391–398, Sept., 1960. 3 figs., 33 refs.

A study of the metabolism of thyroid hormones in 19 euthyroid but mentally retarded children aged 3 to 9 years is reported in this paper from the National Institutes of Health, Bethesda, Maryland. Serum protein-bound iodine levels and thyroxine-binding capacity were found to be within the normal range. Radioactive thyroxine and triiodothyronine were administered and their rate of disappearance from the body was estimated. The mean half-life of thyroxine was 4·95 days and of triiodothyronine 1·13 days, indicating a faster rate of metabolism of the latter.

These findings indicate that children have an increased rate of utilization of thyroid hormones, and that in the case of triiodothyronine this is 3 times greater in the child than in the adult. *R. M. Todd*

589. **Idiopathic Epilepsy in Early Infancy. The Question of Frequent Daily Attacks Causing Undifferentiated Type of Mental Deficiency**
A. DEKABAN. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **100**, 181–188, Aug., 1960. 4 figs., 6 refs.

The author set out to examine the hypothesis that frequent attacks of epilepsy in infancy can cause severe mental retardation, and in this paper from the National Institutes of Health, Bethesda, Maryland, he describes the findings in 6 patients, aged 9 to 39 months, in whom daily epileptic attacks began before they were 6 months old. Comprehensive neurological and biochemical investigations failed to show any organic or metabolic disorder. The pneumoencephalographic findings were normal, but the electroencephalogram was abnormal in all 6 cases. There was a family history of convulsive disorders in 3 cases. Only one infant had major seizures, the other 5 having various types of minor attack with great frequency. In all the infants development was normal until several weeks after the onset of the fits, when marked regression was noted until the frequency of the fits was controlled by drugs. In one case the seizures could not be controlled.

The author states that the clinical and laboratory data, which are given in a table, suggest that idiopathic epilepsy can occur in infants under one year of age, and that the results of detailed investigations carried out are " compatible with the hypothesis that frequent daily epileptic attacks under one year of age can lead to serious and, at times, irreversible mental retardation ", such attacks hampering the infant's alertness and delaying learning and progress.

An epidemiological study is in progress which may either corroborate or disprove this hypothesis.
M. R. Medhurst

590. **Treatment of " Hypsarrhythmia " with ACTH.** [In English]
W. TROJABORG and P. PLUM. *Acta paediatrica* [*Acta paediat. (Uppsala)*] **49**, 572–582, Sept., 1960. 8 figs., 17 refs.

The term " hypsarrhythmia " has been applied to the type of infantile spasm which is associated with a characteristic electroencephalogram (EEG). The prognosis is extremely poor; 10% of affected children die within the first year of life and 90% become mentally defective. The spasms consist of a series of jerks which vary in number from 2 or 3 to 70 and as many as 10 attacks can occur in one day. The attacks usually start between the age of one month and 13 months and cease spontaneously at about 3 to 4 years of age. At Rigshospitalet, Copenhagen, the authors studied the response to adrenocorti-

cotrophin (ACTH) in 30 children (22 boys and 8 girls under 18 months of age) suffering from hypsarrhythmia. Of these patients, 7 died before the age of 3 years and of the remaining 23, 19 are mentally defective and the other 4 suspected of being so. Cerebral palsy was present in 13 patients, and in the 25 in whom air encephalography was performed there was evidence of cortical and ventricular atrophy. The EEG showed large slow waves and asynchronous spikes. At necropsy on 4 patients diffuse extensive cortical and subcortical degenerative and destructive processes were found.

Treatment was with 5 to 10 units of ACTH daily for 3 to 4 weeks. Of the 22 patients so treated 7 showed definite clinical benefit, the attacks becoming fewer or ceasing and, in 4, a normal EEG. This was associated with some improvement in intelligence, which, however, never became normal. In 3 patients there was an effect on the EEG only, while in 12 no clinical or EEG improvement was observed. The authors emphasize that a beneficial effect can be expected only if treatment is started early. *N. S. Alcock*

591. **Psychopathological Peculiarities of Children with Premature Puberty and Growth Development and Acquired Cerebral Deficiency.** (Психопатологические особенности детей с преждевременным половым и физическим созреванием в связи с приобнетенной чедостаточностью центральной нервной системы)
K. S. Vitebskaja. *Журнал Невропатологии и Психиатрии* [*Ž. Nevropat. Psihiat.*] **60**, 876–881, No. 7, 1960. 21 refs.

Macrogenitosomia praecox is a clinical symptom complex found in diseases of diverse aetiology and pathogenesis, and has been classified as idiopathic, endocrinal, and cerebral. It is with the cerebral type that the present paper deals, the patients being 18 girls and 2 boys. In most of these children the intellectual development was normal, and their poor scholastic results were due to lack of mental activity or to lack of interest in school work. Psychiatric observation led to their being placed in two groups.

The first group, consisting of 10 girls and the 2 boys, showed a mental capacity within normal limits, and most of them came under observation for asthenia or various vegetative symptoms. They were subject to irritability, aggressive attacks, and passionate outbursts, being at the same time timid and hypochondriacal. They were often terrified of medical treatment, were lachrymose and complaining, and were always on the look-out for slights, suffering much from the mockery of their young associates on account of their physical abnormalities and backwardness at school. There was no tendency to overt sexual acts, but most of them showed slight coquettishness, an excessive interest in erotic literature and films, and a love of self-adornment. Even those of poor intellect showed practical ability and interest in domestic affairs and work, and their interests centred upon home and family.

The second group (8 girls), on the other hand, evinced a definite pathological mental state; there was a definite proclivity to erotic behaviour, leading to trouble with the police and law-courts. Besides this, there was a tendency to thieving, lying, and sadistic cruelty to other children; also greediness, especially for sweets, and the telling of "dirty" stories were common. These patients were difficult both in the home and in hospital, being rude and insubordinate, foul-mouthed, and liable to encourage other children to behave in the same way. Early menstruation and rapid bodily growth were followed by a period of retarded growth, causing them to become short in stature, with long bodies and short limbs. "Blackheads" and spots on the face and lineae striatae on the trunk were common. There was neurological evidence of poor convergence of the eyes, asymmetry of the mouth on smiling, and inequality of tendon reflexes. Vegetative paroxysms, in the form of asthma, palpitation and tachycardia, sweating, sudden muscular hypotonia or rigidity, paraesthesiae, or headaches were common in these children, while often there were also disturbances of appetite, intense thirst and polyuria, subfebrile temperature, and abnormal glucose tolerance, suggestive of endocrine abnormalities.

In both groups the history revealed in many cases a pathological pregnancy or birth, asphyxia neonatorum, and repeated severe infections, especially dysentery (in no fewer than 14 cases). Cerebral trauma had occurred in 3 cases. Treatment was based on institutional control and re-education, combined with drugs such as "aminazine" (chlorpromazine) to lower the irritability of the vegetative centres. It is pointed out that children in the second group, with their behaviour defects and antisocial outlook, present a much more serious problem, and only prolonged institutional treatment can prevent them from becoming a menace to themselves and to other children. *L. Firman-Edwards*

592. **Prognosis of the Eczema–Asthma Syndrome**
D. Burrows and R. W. B. Penman. *British Medical Journal* [*Brit. med. J.*] **2**, 825–828, Sept. 17, 1960. 2 figs., 10 refs.

The prognosis and the respiratory complications in infantile eczema were studied in 43 children with eczema admitted to the Belfast City Hospital 9 to 12 years previously, when under 2 years of age. Of the 38 children who were traced true infantile eczema had been diagnosed in 29, and 24 of these still had eczema. The respiratory complications were assessed in 20 of the 29 living near the hospital, these being divided into 4 groups according to the severity of past symptoms. Ventilatory capacity, determined by measuring forced expiratory volume over one second, and vital capacity before and after inhalation of an adrenaline–atropine spray were recorded. A history of respiratory disorders was noted in 16 children, but the condition was mild in 6 of them. Thus, the incidence of severe respiratory trouble in this group (10 out of the 20 cases) was 50%. A significant diminution in ventilatory capacity was demonstrated only in children with the most severe symptoms. There was a tendency for the more severe respiratory symptoms to develop later in life than the mild symptoms. Of the 5 children who no longer had eczema 2 had asthma.
E. H. Johnson

Medical Genetics

593. **The Syndrome of Sporadic Goitre and Congenital Deafness**

G. R. Fraser, M. E. Morgans, and W. R. Trotter. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **29**, 279–295, April [received Aug.], 1960. 6 figs., 33 refs.

The authors of this paper from University College Hospital Medical School, London, observed the syndrome of goitre and congenital deafness in 28 individuals from 18 families. The syndrome appeared to be inherited as a mendelian recessive character. The main feature of the thyroid abnormality was inability to form organic iodine compounds at a normal rate. Affected and unaffected members of the families were studied following administration of potassium chlorate one hour after an oral dose of radioactive iodine (^{131}I). In all the congenitally deaf subjects the ^{131}I in the thyroid was partially discharged by the perchlorate. Some of the affected subjects were hypothyroid but most were euthyroid. Audiograms revealed severe high-tone deafness in all the subjects who reacted in this way to perchlorate. This was apparently not caused by hypothyroidism, but appeared to be an independent expression of the genetic abnormality. *H. Harris*

594. **Sex-linked Deafness of a Possibly New Type.** [In English]

J. Mohr and K. Mageröy. *Acta genetica et statistica medica* [*Acta genet. (Basel)*] **10**, 54–62, 1960. 1 fig., 6 refs.

There is evidence that the most common means of inheritance of genetically determined deafness is either by autosomal recessive genes of complete penetrance or by autosomal dominant genes of high but incomplete penetrance (*Ann. hum. Genet.*, 1956, **20**, 177; 1959, **23**, 357). In a small proportion of individuals with genetically determined deafness a sex-linked mode of inheritance may operate, and this may explain the slight preponderance of males among deaf-mutes.

The authors review earlier data on sex-linked deafness, and then describe their findings at the University Institute of Human Genetics, Oslo, in the case of a Norwegian family in which there were 11 male deaf-mutes in 4 successive generations. The 6 sibships concerned comprised 18 females and 17 males. In each family with affected sons both parents were unaffected, and the connexion with the affected kindred was through the mother. None of those affected had children. The most probable genetic hypotheses to explain these data are those of (*a*) sex-linked recessive inheritance, and (*b*) autosomal dominance with sex-limitation to males. The authors point out that the only way of differentiating between the two is by consideration of offspring of affected males or by the theoretical possibility of demonstrating linkage with a known sex-linked trait. In default of information from such sources they suggest that the most likely hypothesis is that deafness in this family is due to sex-linked inheritance.

Reports of objective assessments of hearing and speech in the early years of life of affected individuals were lacking; but from information supplied by relatives about early development of speech there was good evidence in 5 cases that the deafness was progressive. The authors therefore suggest that the condition should be designated " progressive sex-linked deafness ". *R. H. Cawley*

595. **Laboratory and Genetic Observations in Another Family with the Hageman Trait**

J. H. Thompson Jr., J. A. Spittel Jr., C. A. Pascuzzi, and C. A. Owen Jr. *Proceedings of the Staff Meetings of the Mayo Clinic* [*Proc. Mayo Clin.*] **35**, 421–427, July 20, 1960. 1 fig., 11 refs.

The Hageman trait, or lack of the so-called Hageman factor, is characterized by abnormally prolonged clotting time of whole blood without any bleeding tendency. In only 3 reported instances has this rare abnormality been observed in more than one member of a family. In this paper from the Mayo Clinic, the authors describe a fourth family in which 2 sisters and a brother were affected. Another sibling, the parents, and 8 other members of the family were tested and found to be unaffected. The parents were not known to be blood relations, but all 4 grandparents went to the United States from neighbouring communities in Norway. Electrophoretic studies of normal plasma showed that the Hageman factor was associated with the zone occupied by gamma-globulin on paper strips.

The authors note that subjects known to have Hageman's trait are rarely available for direct comparison with individuals suspected of having the trait, and they suggest that avian plasma may be helpful. Blood from ducks, pigeons, turkeys, geese, and chicken failed to shorten the clotting time of plasma from individuals with Hageman's trait. Normal human plasma shortened the prolonged clotting time of the plasma of these birds but plasma from individuals with Hageman's trait did not do so. *C. O. Carter*

596. **Hereditary Haemorrhagic Telangiectasia: a Study of a Family with Six Children**

V. R. Bloom and E. J. Moynahan. *British Journal of Dermatology* [*Brit. J. Derm.*] **72**, 312–317, Aug.–Sept., 1960. 3 figs., 16 refs.

The authors describe a study of a family of 6 children, one of whom had hereditary haemorrhagic telangiectasia. The patient, a girl aged 4½ years, was referred to the Hospital for Sick Children, Great Ormond Street, London, because of a lesion on the face resembling a port-

wine stain but distinguishable by being raised and capable of obliteration by pressure. She also had a spider lesion on the back of one hand and a pinpoint lesion on each ear. It was found that the father and the 5 siblings were also affected. The two eldest children, girls aged 15 and 12 years, had fits with electroencephalographic evidence of focal brain lesions. The authors discuss the possibility that these fits are manifestations of the disease. *C. O. Carter*

597. **Haemoglobin O in an Arab Family: Sickle-cell Haemoglobin O Trait**
B. RAMOT, S. FISHER, D. REMEZ, R. SCHNEERSON, D. KAHANE, J. A. M. AGER, and H. LEHMANN. *British Medical Journal* [*Brit. med. J.*] **2**, 1262–1264, Oct. 29, 1960. 5 figs., 7 refs.

598. **The Chromosome Complement in True Hermaphroditism**
M. A. FERGUSON-SMITH, A. W. JOHNSTON and A. N. WEINBERG. *Lancet* [*Lancet*] **2**, 126–128, July 16, 1960. 2 figs., 14 refs.

Recent advances in cytological techniques have made it possible to test the hypothesis that abnormalities of the chromosome sex-determining mechanism in man cause human intersexuality. The authors of this paper from the Johns Hopkins University School of Medicine, Baltimore, and the National Institutes of Health, Bethesda, Maryland, describe 2 cases of true hermaphroditism in which a sex chromosome constitution XX was demonstrated. They refer to 2 similar cases reported by Hungerford *et al.* (*Amer. J. hum. Genet.*, 1959, **11**, 215) and Harnden and Armstrong (*Brit. med. J.*, 1959, **2**, 1287; *Abstr. Wld Med.*, 1960, **28**, 165).

The first patient, who had been brought up as a boy, had ambiguous external genitalia—one ovary, one testis, an under-developed uterus, one fallopian tube, and a rudimentary prostate gland. Histological examination of buccal smears and of material obtained at laparotomy showed that the cells had a single sex chromatin body. Culture of bone-marrow cells revealed a modal chromosome number of 46, although 12·6% of cells contained 45 chromosomes and 18·5% contained 47. In none of the cells analysed was a Y chromosome seen. The authors discuss the possibility that this patient was indeed an XXX/XX mosaic, but do not favour this interpretation because of the absence of double sex chromatin bodies and also the lack of clinical features which they associate with an XXX sex chromosome constitution.

The second patient had also been brought up as a boy and had ambiguous external genitalia. There was an ovotestis on one side of the bifid scrotum and on the contralateral side of the body there was a normally situated ovary with fallopian tube. The nuclear sex was chromatin positive. In this case, too, the modal chromosome number was 46, but without excess of non-modal cells. On analysis, the sex chromosome constitution was found to be XX.

The authors discuss the implications of these and other published findings in true hermaphroditism with respect to the problems of sex determination and differentiation. They conclude that either there is an unobserved chromosomal aberration in these cases or that sex differentiation has been disturbed by some factor acting on the anlage of one undifferentiated gonad. *A. G. Baikie*

599. **Chromosomal Constitution and Nuclear Sex of a True Hermaphrodite**
L. M. DE ASSIS, D. R. EPPS, and C. BOTTURA. *Lancet* [*Lancet*] **2**, 129–130, July 16, 1960. 4 figs., 8 refs.

The authors describe the results of chromosomal counts and the determination of nuclear sex in a true hermaphrodite.

The patient, who was admitted to the Hospital das Clinicas, São Paulo, Brazil, at the age of 14, had been brought up as a boy in spite of ambiguous genitalia and perineal hypospadias. He was found to have a urogenital sinus, vagina, uterus, ovary, and fallopian tube on one side only; in the inguinal region on the other side was an ovotestis. Buccal smears were chromatin positive. The chromosomal constitution was studied in bone-marrow cells obtained after intravenous administration of colchicine. In 25 cells examined the chromosome number was found to be 46. There were 16 cells suitable for analysis and in none was a Y chromosome seen. These analyses were consistent with a sex chromosome constitution XX, and similar to those in all reported cases of true hermaphroditism in which chromosome studies have been carried out. *A. G. Baikie*

600. **A Child with 49 Chromosomes**
M. FRACARRO, K. KAIJSER, and J. LINDSTEN. *Lancet* [*Lancet*] **2**, 899–902, Oct. 22, 1960. 5 figs., 16 refs.

601. **Pheochromocytoma as an Inherited Abnormality: Report of the Tenth Affected Kindred and Review of the Literature**
C. T. CARMAN and R. E. BRASHEAR. *New England Journal of Medicine* [*New Engl. J. Med.*] **263**, 419–423, Sept. 1, 1960. 1 fig., 24 refs.

Remarking that the familial occurrence of phaeochromocytoma has received relatively little attention, the authors describe a family in which father, son, and daughter were affected. The father died of intracranial haemorrhage at the age of 57 years, and the diagnosis of bilateral phaeochromocytoma was made at necropsy. The 2 children were both treated surgically at the University of California Medical Center, San Francisco, the daughter at the age of 17 years by removal of the left adrenal gland, and the son at the age of 22 years by removal of the right adrenal gland. Both have remained well for the past 3 years.

The authors have been able to collect 9 other instances of phaeochromocytoma occurring in more than one member of a family. In these families the pattern of inheritance is compatible with causation by a dominant gene, and in the affected members it is common for symptoms to recur because of a functioning tumour in the other adrenal or at another site in the gland originally affected. *C. O. Carter*

Public Health and Industrial Medicine

602. **Natural Radioactivity in West Devon Water-supplies**

J. D. ABBATT, J. R. A. LAKEY, and D. J. MATHIAS. *Lancet* [*Lancet*] **2**, 1272–1274, Dec. 10, 1960. 2 figs., 2 refs.

Wide variations in the natural radioactive content of water-supplies have been demonstrated in West Devon and elsewhere. Unexpected variations in cancer incidence, apparently related to water-supplies, have also been reported in West Devon. An intensive programme of measurement of radioactivity and a social survey is now being conducted in West Devon to try to define the extent of individual exposure in the area to radiation and to any other agents in the water, and to relate this exposure to any effects that may be produced.—[Authors' summary.]

603. **Study in the Efficiency of Vaccination against Influenza in Two Employment Groups in Melbourne in 1959**

A. E. DUXBURY and T. E. B. KEEN. *Medical Journal of Australia* [*Med. J. Aust.*] **2**, 206–208, Aug. 6, 1960. 5 figs., 7 refs.

The authors of this paper from the Commonwealth Serum Laboratories, Parkville, Victoria, Australia, point out that it is now possible to detect fairly accurately the dates of onset and cessation of epidemic influenza in any area served by a virus laboratory because of the efficient techniques used for isolating viruses and testing for antibodies against type-specific (S) and species-specific (V) antigens. Studies of the efficacy of an influenza vaccine should therefore be restricted to the periods when it can be shown that the subjects have been exposed to risk.

During a widespread epidemic of virus A/Asian influenza in Australia in 1959 the authors studied the efficacy of a polyvalent influenza vaccine, made up of four different types of influenza virus A, one type of virus B, and one of virus D (Sendai), in the employees of two large organizations (A and B). Patients who had been vaccinated against influenza the previous year received a booster dose and those with no previous vaccination received 2 doses. Vaccination was carried out in April and continued in some instances until the first week of May. In December all the subjects were asked to supply details of respiratory illness and of absence from work during the preceding 12 months, together with any history of previous vaccination against influenza. The number of days lost due to influenza and similar diseases was calculated for each subject. There was a marked rise in the incidence of influenza and other respiratory illnesses in May in both groups of employees, with a lesser rise in July in Group A. Each group was divided into (1) those considered to be adequately immunized and (2) those not, or at least not sufficiently, protected, the numbers in each sub-group being: Group A 487 and 896 respectively, and Group B 355 and 197 respectively.

Although in 1959 the influenza epidemic had started earlier than usual the polyvalent vaccine gave significant protection to the vaccinated subjects in both groups in May and to those in Group A in July (89%), but not to those in Group B in that month. There was no evidence of the circulation of any influenza-type illness in July, but haemadsorption viruses were known to be present and since these are antigenically related to Sendai viruses (one of the components of the vaccine) the authors consider that infection due to this type may explain the rise. [It does not.] The protection rate in May was about 60%.

[In spite of the disparity in numbers of the non-protected subjects in the two groups it seems that, with the exception of Group A in July, the experience at both work-places A and B was practically the same for the rest of the year. In July the unprotected subjects in Group B lost fewer working days per month than the protected. Having regard to the high degree of urbanization in Melbourne, the possible presence of haemadsorption viruses in July does not explain why Group B should have been unaffected if the two groups were comparable otherwise. If the polyvalent vaccine really gave some protection in May the authors seem to have been extremely skilful in giving the appropriate injections at exactly the right time.] *W. K. Dunscombe*

604. **A Contact-plate Technique for Determining Bacterial Contamination of Fabrics**

S. D. RUBBO and S. DIXSON. *Lancet* [*Lancet*] **2**, 394–397, Aug. 20, 1960. 5 figs., 5 refs.

The bacterial contamination of fabrics is an important factor in the causation of cross-infection in hospitals. This paper from the University of Melbourne describes a contact-plate technique for determining the degree of contamination of all types of textiles and compares its efficiency with that of 2 other sampling methods. Of the 3 methods the sweep-plate technique of Blowers and Wallace (*Lancet*, 1955, **1**, 1250; *Abstr. Wld Med.*, 1956, **19**, 162) was the least satisfactory. There was a tendency for the colonies to become crowded at the periphery of the plates and for variations in the counts to occur due to uncontrollable factors. The contact-plate method, in which the fabric was sandwiched between the medium and an applicator, gave much better spacing of colonies, more regular results, and, particularly with cotton fabrics, a better approximation of the actual number of organisms on the fabric. A modification of the percussion-plate technique of Puck *et al.* (*Amer. J. Hyg.*, 1946, **43**, 91) was also employed. With this method the fabric was tightly stretched over a culture plate and organisms were dislodged on to its surface by the im-

pingement of a steel ball dropped from a height. Plates prepared in this way were considered to provide better evidence of the number of bacteria likely to be dislodged from fabrics as a result of agitation than could be obtained from sweep plates. *R. Hare*

605. **Vehicles of Transmission of Airborne Bacteria in Hospital Wards**
S. D. RUBBO, T. A. PRESSLEY, B. C. STRATFORD, and S. DIXSON. *Lancet* [*Lancet*] **2**, 397–400, Aug. 20, 1960. 2 figs., 10 refs.

The authors of this paper from the University of Melbourne have studied the methods by which air-borne bacteria are transmitted in hospital wards. Such bacteria may be attached (1) to droplet nuclei which have originated from the nasopharynx of a patient; (2) to "fibre nuclei", which consist of minute particles which float freely in the atmosphere; or (3) to large fibres, which settle very quickly and become resuspended only as a result of agitation. Counts obtained on settling plates placed at floor level and at 3, 6, and 9 feet (0·9, 1·8 and 2·7 metres) above that level showed that staphylococci were present in approximately equal numbers at all levels. Fibre counts, on the other hand, showed that the numbers present were considerably greater at floor level and at 3 feet (0·9 m.) than at the higher levels. It was also found that the fibres were mostly composed of cellulose. The authors conclude that staphylococci in the air of wards are not attached to large wool fibres, but to cellulose fibre nuclei arising mainly, but not necessarily exclusively, from cotton sheeting. Droplet nuclei play only a minor part in contaminating a ward environment. *R. Hare*

606. **A New Technique for the Control of Hospital Cross-infection. Experiences with BRL.1241 in a Maternity Unit**
S. D. ELEK and P. C. FLEMING. *Lancet* [*Lancet*] **2**, 569–572, Sept. 10, 1960. 4 figs., 8 refs.

The spraying into the atmosphere of a concentrated solution of an antibiotic active against all strains of pyogenic staphylococci should produce droplet nuclei of the antibiotic, which would follow essentially the same pathways as the staphylococci in the environment. If an adequate concentration could be achieved on the nasal mucosa, the main source of staphylococci would be cut off, and the concentration of staphylococci in the surroundings would gradually diminish. This in turn should lead to a reduction in cross-infection.

This hypothesis was tested in the maternity unit of St. George's Hospital, London, methicillin ("celbenin"; BRL.1241), a synthetic derivative of 6-aminopenicillanic acid, being used. All parts of the ward and nursery were sprayed once a day with 1 g. of the drug dissolved in 20 ml. of distilled water; this resulted in a reduction in the percentage of positive cultures of *Staphylococcus pyogenes* from infants' nasal swabs from 50 to 24. Spraying with 1 g. 4 times a day was associated with a reduction to 12·4%, and, in a further group of 29 infants, there were only 6 positive cultures from 290 nasal swabs, suggesting a cumulative effect. Over a period of 6 months 340 infants were born, approximately equally divided between a treated and an untreated ward. In the untreated ward there were 14 minor lesions from which *Staph. pyogenes* was cultured; no such lesions were observed in the treated ward, where spraying with 4 g. of the drug was carried out daily over the whole period, although the infants in both wards were looked after by the same nurses. After 6 months' spraying the dust in the test ward was found to have an inhibitory activity corresponding to 200 μg. of methicillin per g. of dust.

No hypersensitivity phenomena were observed in the infants, mothers, or nurses. Nasal swabs from the nurses failed to reveal the carriage of staphylococci resistant to methicillin. The method is economical in labour and materials and is recommended as a basis for further research into the prevention of staphylococcal cross-infection. *H. Caplan*

607. **Staphylococcal Sepsis in Out-patients. Relation of Penicillin Resistance to Previous Contact with Hospitals**
D. A MACFARLANE, J. S. MURRELL, R. A. SHOOTER, and M. P. CURWEN. *British Medical Journal* [*Brit. med. J.*] **2**, 900–902, Sept. 24, 1960. 9 refs.

Coagulase-positive staphylococci were isolated from the lesions of 170 out of 208 out-patients with acute infections of the skin and subcutaneous tissues attending the casualty department of St. Bartholomew's Hospital, London, between October, 1959, and March, 1960. Of these organisms, 67 strains (39%) were resistant to penicillin. In 1950 only 6% of the strains isolated from the department were penicillin-resistant; in 1952, 16%; in 1955, 21%; and in 1957, 25%.

Of the 94 patients who had a personal or family history of hospital attendance during the preceding 12 months, 52% had penicillin-resistant staphylococci, compared with 24% of the 76 patients with no such contact. This, it is suggested, is a further illustration of the part played by hospital infection in seeding the population with antibiotic-resistant staphylococci.

It was found that 71% of the 170 septic patients were nasal carriers of coagulase-positive staphylococci, compared with 34% of 214 non-septic casualty patients. That the staphylococci in the nose and in the lesion may in most cases have been of the same strain is suggested by the observation that only 13 (8%) of the patients had a sensitive organism in the nose and a resistant one in the lesion, or vice versa. *H. Caplan*

608. **Incidence of Surgical Wound Infection in England and Wales**
A REPORT OF THE PUBLIC HEALTH LABORATORY SERVICE. *Lancet* [*Lancet*] **2**, 659–663, Sept. 24, 1960. 3 refs.

In the course of a planned investigation of the incidence of postoperative wound sepsis a total of 3,276 patients operated upon in 21 different hospitals were studied clinically, while bacteriological examination was undertaken during convalescence in 2,860 of these cases. The hospitals were selected on the basis of convenience.

Of the 2,746 wounds for which there was complete clinical and bacteriological information, 308 (11%) were septic and yielded pathogenic bacteria. Almost half the

wounds reported as septic discharged pus at some time, and only 59 (16%) had no more than a stitch abscess or marginal erythema. *Staphylococcus aureus* was found in 229 (60%) of the septic wounds and in 202 (9%) of the healthy wounds. Coliform organisms were found in 115 (30%) of the septic wounds, in 50 of them in association with staphylococci.

The sepsis rate in different hospitals undertaking general surgery was between 4·7% and 21·8%. The highest sepsis rates after clean operations were for cholecystectomy (21%) and breast operations (15%), and the lowest for orthopaedic operations (2%). Increased age of patient, length of incision, and duration of operation were all associated with a higher sepsis rate.

Nasal carriers of *Staph. aureus* had only a slightly higher postoperative sepsis rate than non-carriers (8·9% compared with 7·1%), but of the 74 patients who carried phage-types 80, 52/52A/80, or 52/80 in the nose before operation, postoperative sepsis developed in 11 (14·9%), in 10 cases with a staphylococcus of the type found in the nose.

Patients with wound sepsis stayed in hospital, on an average, 7·3 days longer than predicted on the day of operation. Of the patients in the survey 58 died, but in only one case was death definitely attributable to wound sepsis.

If the figures of this survey are applicable to the 1·5 million surgical operations performed annually in England and Wales the total excess stay in hospital due to sepsis may be about 1,000,000 days per year, or about 3% "of the total bed-occupancy of acute hospitals".

The authors conclude that one should " regard as a challenge to our medical skills the thought of 75,000 people who had clean operation wounds that discharged pus, of the 5,000 whose stay in hospital was prolonged by a month or more, and of the, perhaps, 500 who died from sepsis ". *H. Caplan*

INDUSTRIAL MEDICINE

609. **Mica Dust as an Occupational Hazard.** (Материалы к гигиенической характеристике пыли слюды)

I. K. Puškina. *Гигиена и Санитария* [*Gig. i Sanit.*] **25**, 18–23, Aug., 1960. 4 figs., 9 refs.

As part of an investigation of the effect of mica on the health of workers in the electrical insulator industry, the author reports experiments performed on white rats to ascertain the action of mica (muscovite and phlogopite) on the lungs. Measurement in the factory of dust concentrations of up to 100 mg. per c. metre showed that most of the particles (68%) were less than 10 μ in diameter. Mica particles are in the form of needles or small plates. Mica dust in which 90·8% of the particles were less than 6 μ in diameter was injected intratracheally into the rats in a single dose of 50 mg. in 0·6 ml. physiological saline and the animals killed for examination 4, 6, and 8 months later. The only organs to show pathological changes were the lungs, and in these the changes caused by both types of mica were identical. Focal granulomata with a marked giant-cell reaction and a moderate focal or diffuse sclerosis with disturbance of the lymph or blood flow were observed. There was no exudate, and phagocytosis of the dust was in process.

Medical and radiological examination of the chest of workers engaged in the manufacture of insulators revealed the presence of early pneumoconiosis in 3 and of suspected pneumoconiosis in 5 out of 22 workers aged under 50 years and with a working history of over 5 years. Various measures designed to prevent the development of pneumoconiosis among workers exposed to mica dust are suggested. *Basil Haigh*

610. **Initial Changes in the Human Lung Due to Dust Containing Silica.** (Начальные изменения в легких людей под влиянием пыли, содержащей двуокись кремния)

P. P. Dvižkov and L. I. Ěl'jašev. *Гигиена Труда и Профессиональные Заболевания* [*Gig. Truda prof. Zabolev.*] **4**, 17–23, Aug., 1960. 6 figs.

With the increasing effectiveness of measures for the prevention of silicosis the diagnosis of early (and therefore possibly reversible) forms of the disease has become important. This report describes the post-mortem findings in young miners with short (6 months to 4 years) exposure to dust, in concentrations of not more than 5 or 6 mg. per c. metre, who had died from causes other than silicosis.

Changes interpreted as initial stages of silicosis were found in the lungs and regional lymph nodes and consisted in the accumulation of dust in the form of miliary foci around the bronchi and vessels, in the lumen of the alveolar ducts, and in the alveoli themselves, with the development of connective tissue fibres between the cells. Other manifestations of sclerosis were an increase in the connective tissue around the vessels and bronchi, thickening of the interalveolar septa, changes in the bronchi, focal emphysema, and appreciable sclerosis of the regional lymph nodes. These changes were not demonstrable radiologically, although they could be correlated with disturbances of respiratory function. *Basil Haigh*

611. **Bronchial Asthma in the Aluminium Industry.** [In English]

O. Midttun. *Acta allergologica* [*Acta allerg.* (*Kbh.*)] **15**, 208–221, 1960. 2 figs., 20 refs.

The results of an investigation into the causes of the prevalence of bronchial asthma in workers in the aluminium industry in Sunndalsøra, Norway, are described. Aluminium is manufactured in special electrolytic cells or pots. Pot-room workers suffer much irritation of mucous membranes as a result of dust, fumes, and smoke. The fumes of the aluminium do not cause asthma, but in the pot-room atmosphere, which has a high fluorine content, asthma tends to develop in many of the workers after a 3-year exposure period. It is presumed that asthma occurs in pot-room workers in other countries, though this has not been reported, and the author recommends the wearing of gas masks as a prophylactic measure. *A. W. Frankland*

Forensic Medicine and Toxicology

612. **The Habitual Criminal. Observations on Some of the Characteristics of Men Sentenced to Preventive Detention**
R. S. TAYLOR. *British Journal of Criminology* [*Brit. J. Crim.*] **1**, 21–36, July, 1960.

Some characteristics of 100 men sentenced to preventive detention and admitted consecutively to Wandsworth Prison, London, during 1956 are described. All the men were by definition recidivists under detention for not less than 5 years.

The mean age was 40·4 years, S.D. ±8·5 years, and the mean number of previous convictions was 16·5, S.D. ±5·23; all except 4 had been last convicted less than 2 years before the current sentence. Of the 100 men 72 were thieves or housebreakers; judged by the value of the property stolen the offences were comparatively trivial. Some went to the police spontaneously and confessed, others committed the offences in such a way as to make detection certain. The majority were single, divorced, or separated; 15 were married, but some of these marriages were tenuous unions and had been so for many years. A history of physical or mental illness was common. There was a history of meningitis, epilepsy, or chorea in 5 of the men, and 14 had been in mental hospitals. The most outstanding characteristic of the group was social isolation and ineptitude, although the intelligence range was normal; (mean I.Q. 97·4, S.D. ±19·7). Curiously, only a minority of these men had been offenders as juveniles. The incidence of crime among the prisoners' relatives was low; thus, of 357 siblings only 6 had had convictions. Altogether 54 of the men came from " disturbed " parental homes, and most of those who were juvenile offenders were found in this group.
D. J. West

613. **Suicide: The Influence of Organic Disease**
I. STEWART. *Lancet* [*Lancet*] **2**, 919–920, Oct. 22, 1960. 2 refs.

The author suggests that the lay public, and to a lesser extent the medical profession, believe that suicide is precipitated by disturbance of the mind alone. He agrees that psychiatric factors play an important part, but points out that organic disease often helps to prepare the way for the act. As coroner's pathologist in the area of Keighley, Yorkshire, he examined between 1952 and 1959 a total of 122 subjects who had committed suicide.

Only 37 of these had no organic disease, while 33 had hypertension with cardiac hypertrophy, which, the author claims, is a familiar accompaniment of depression. Peptic ulcer or gastritis was present in 10 of the 122 subjects, other conditions including gross obesity in 21, gall-stones in 8, carcinoma in 3, and anaemia in 2. The author points out that while it is impossible to assess the influence of the physical disease on suicide in these subjects it is clear that they were on the whole seriously ill or unfit.
Gavin Thurston

614. **Treatment of Severe Acute Barbiturate Poisoning by Forced Diuresis and Alkalinisation of the Urine**
N. A. LASSEN. *Lancet* [*Lancet*] **2**, 338–342, Aug. 13, 1960. 6 figs., 19 refs.

It is pointed out that while the prognosis in acute barbiturate poisoning has considerably improved over the last 10 years, increasing the rate of excretion of the drugs from the body can improve the prognosis still further. At Bispebjerg Hospital, Copenhagen, this was achieved by forced diuresis and alkalinization of the urine, the method being as follows. Urea in a 15% isotonic solution containing sodium lactate was given intravenously until the patient was sufficiently conscious to say " yes " and " no ", when fluids were given by mouth; to hasten alkalinization, if necessary, sodium bicarbonate solution was also given subcutaneously. The output of urine and the blood chemistry and barbiturate levels were determined. Of 14 patients treated, all of whom had unusually high serum barbiturate levels, 13 recovered after forced diuresis and alkalinization of the urine; the remaining patient died, a large pulmonary embolisim being found at necropsy. The average duration of treatment was 42 hours. Complications included increased venous pressure and, in one case, dehydration from excessive diuresis, for which a glucose solution was considered responsible; during the phase of dehydration intracranial haemorrhage occurred.

The rate of excretion of the different barbiturates varied, and the author found it difficult to estimate the probable duration of unconsciousness if the drug had not been completely absorbed from the alimentary tract. In all cases the period of unconsciousness, compared with that in controls, was shortened to about one-third, and the rate of fall in the blood barbiturate level was always accelerated. It is emphasized that this treatment is an adjuvant and not an alternative to established procedures. The risks of overloading the circulation and of dehydration must be carefully weighed against the benefits to be expected.

[The original paper should be consulted by those interested in the details of the author's technique.]
Gavin Thurston

615. **The Prompt Treatment of Salicylism with Sodium Bicarbonate**
T. K. OLIVER JR. and M. E. DYER. *A.M.A. Journal of Diseases of Children* [*A.M.A. J. Dis. Child.*] **99**, 553–565, May, 1960. 6 figs., 30 refs.

The results of administration of sodium bicarbonate in acute salicylism in children who had accidentally taken an overdose of salicylates is described in this paper

from the Children's Hospital, Columbus, Ohio. It is pointed out that there is no specific antidote for salicylism, but as the *p*H of the urine rises, excretion of salicylates increases. A total of 38 affected children (aged 14 to 48 months) were given an emetic on admission to hospital and the serum salicylate level was determined. The serum *p*H and carbon dioxide content were also determined serially in 29 of the children. The patients were divided into three groups as follows: Group 1 (12 patients) received water and carbonated beverages by mouth and 0·3% sodium chloride in 6·6% dextrose solution intravenously; the daily fluid intake amounted to over 3 litres per square metre of body surface a day, of which one-half was given within the first 8 hours. Group 2 (18 patients) were given in addition to the above fluid regimen sufficient sodium bicarbonate intravenously to raise the serum bicarbonate level by 5 to 7·5 mEq. per litre during the first 4 hours. Group 3 (8 patients) received and retained fluids in amounts less than 2·5 litres per square metre of body surface a day.

On the average 5 hours elapsed between the time of ingestion of salicylates and admission to hospital. Hyperventilation, accompanied by tachypnoea, was the commonest sign and was present in 32 patients. Vomiting occurred in 16 patients before the emetic was given and 15 were drowsy, one child being actually comatose. Bicarbonate administration was followed by excretion of an alkaline urine and a fall in the serum salicylate level, which reached a minimum after 6 hours in 15 of the 18 children in Group 2. No appreciable difference was observed between the two control groups in the rate of fall in the serum salicylate level, which was more gradual than in the patients in Group 2. Bicarbonate administration was followed by a small and transient rise in the serum *p*H to a mean of 7·5 after 3 hours. The initial metabolic acidosis was corrected within 14 hours, but the serum potassium level tended to fall during the first 24 hours of treatment. The signs of salicylism disappeared more rapidly in the patients in Group 2 than in the patients in the control groups. No complications were observed. Only in 6 of the 18 patients did the serum salicylate level fail to fall to at least 50% of the pre-treatment value by the end of the first 8 hours. The subsequent course in these children was the same as in the controls.

In the authors' view the rapid fall in the serum salicylate level suggests that careful administration of sodium bicarbonate is the treatment of choice for salicylism in children under the age of 4 years. *Anne Tothill*

616. **Megadolichocolon Due to Lead Poisoning.** (Le mégadolichocolon saturnin)
P. Kissel, L. Collesson, J. B. Dureux, G. Rauber, and D. Anthoine. *Presse médicale* [*Presse méd.*] **68**, 1739–1742, Oct. 26, 1960. 9 figs., 14 refs.

The radiological findings in 2 men, aged 52 and 42 years respectively, who were found to have megacolon associated with lead poisoning are described. In the case of the older patient a high level of lead in the blood was discovered on his second admission to hospital, and this was correlated with the x-ray appearances and the physical signs and symptoms. In the other case a history of working with red lead was not obtained until the patient's third admission to hospital. Both cases were admitted to hospital because of abdominal pain, asthenia, anaemia, loss of weight, and constipation. The first patient had a slight blue line on his gums, and in both cases the abdomen was painful to palpation. Blood levels of lead were 95 and 135 μg. per 100 ml. respectively. In both cases the erythrocyte count was considerably reduced and there was basophilia. [Apparently no blood film was taken in the second case until the third admission to hospital.] Plain radiographs of the abdomen were taken during an acute attack, and further examinations were made after insufflation and the administration of a barium enema. These showed the presence of intestinal loops with gas and fluid levels, distension of the caecum and ascending colon, and dilatation and elongation of the transverse colon extending at times into the descending colon. After treatment with sodium calciumedetate the anaemia and basophilia improved and the x-ray picture became almost normal.

The authors, referring to the work of Levrat *et al.* (*Arch. Mal. prof.*, 1954, **15**, 113), point out that, whereas these workers found that megadolichocolon was only transitory and contemporaneous with the colic crises, this did not apply to the present cases, where the condition was demonstrated on 3 separate occasions some months apart. They believe that the colonic abnormality in cases of lead poisoning can extend considerably beyond the period of colic. They also mention that plain radiographs revealed gas and fluid levels on 2 occasions during an attack of colic, and that the elongation affected both the transverse and sigmoid colons.

In discussing pathogenesis the authors emphasize that neither encephalopathy nor polyneuritis occurred in their cases, and that there was no rise in blood pressure during the crises of colic. They consider that this type of megacolon may represent the effect of lead on the intestinal sympathetic plexuses. They conclude: (*a*) that the increase in calibre of the large intestine may be either segmentary or total; (*b*) that the constipation found in lead poisoning can be explained by the occurrence and persistence of a megadolichocolon; and (*c*) that the x-ray appearances return to normal after treatment with a suitable chelating agent. In their opinion the megadolichocolon accompanying lead poisoning should now be classified as a functional disorder of toxic origin.

[The paper is illustrated with some extremely interesting radiographs.] *W. K. Dunscombe*

617. **Therapeutic Accidents: Adrenaline Poisoning**
H. R. M. Johnson. *Journal of Forensic Medicine* [*J. forensic Med.*] **7**, 198–205, Oct.–Dec., 1960. 1 fig., 22 refs.

Three fatal cases of acute adrenaline poisoning are described, together with a fourth death from haemorrhage into a paraganglioma following palpation prior to laparotomy The pharmacology, uses and toxic effects of adrenaline and noradrenaline are described. The literature relating to adrenaline poisoning is reviewed. Suggestions are made to help reduce the number of such poisonings.—[Author's summary.]

Anaesthetics

618. **Prevention, Diagnosis and Treatment of Prolonged Apnoea**
H. C. CHURCHILL-DAVIDSON and R. P. WISE. *British Journal of Anaesthesia* [*Brit. J. Anaesth.*] **32**, 384–387, Aug., 1960. 3 figs., 5 refs.

The three main muscle relaxant drugs in general use are D-tubocararine chloride (curare), gallamine triethiodide, and suxamethonium chloride. The principles underlying the application of these agents to anaesthetic practice are reviewed by the authors from St. Thomas's Hospital, London. They state that the choice of the particular agent to be employed is mainly influenced by consideration of the length of the operation. The hypotensive effect of curare is undesirable during halothane anaesthesia, and in these cases gallamine is more suitable because it has the advantage of possessing an atropine-like activity which increases the pulse rate.

When respiration is controlled the rapidity with which breathing is initiated depends on three factors: (1) the amount of depression of the respiratory centre; (2) the pCO_2 which, if too high or too low, will fail to stimulate the respiratory centre; and (3) inertia of the centre in the absence of Factors 1 or 2. The first factor can be minimized by avoiding too large doses of premedication drugs, and of thiopentone, intravenous analgesics, and general anaesthetic agents. The second is best controlled by aiming at over-ventilation during maintenance of anaesthesia. In the recovery phase a high flow of gas (14 litres per minute) with the addition of 5% carbon dioxide (CO_2) is preferable to relying on apnoea being prevented by an endogenous rise in pCO_2. If no response is obtained in 5 minutes, the concentration of CO_2 should be reduced to 2%. Inertia is overcome by a surgical stimulus, such as moving the endotracheal tube or deflating its cuff.

Prolonged apnoea (over 10 minutes from completion of the operation) or an inadequate minute-volume may be due to (*a*) depression of the respiratory centre, (*b*) mechanical defects in the respiratory system, or (*c*) peripheral causes (relaxants). The use of a peripheral (ulnar) nerve stimulator is a rapid and certain means of distinguishing (*c*) from (*b*) and from (*a*) because the muscles of respiration always recover their function before the hand muscles. A brief description of different responses to the stimulator is given. If the minute-volume is inadequate, the type of respiration may help in distinguishing the cause. A slow respiratory rate suggests central depression, but a more rapid rate, together with the working of the abdominal and accessory muscles of respiration (and "tracheal tug"), suggests either a mechanical defect in the respiratory system or relaxant effects. A mechanical respiratory defect always calls for x-ray examination to exclude pulmonary collapse or pneumothorax; bronchospasm should be accepted as the cause only after exclusion of these complications.

Treatment essentially consists in trying to keep the oxygen and CO_2 tensions in the blood within normal limits. Emphysema necessitates full laboratory control, because normally this condition gives rise to high pCO_2. Respiratory depression is overcome by administering the appropriate antagonist or a central nervous stimulant. If the peripheral cause is a depolarization block, attempts to improve the cardiac output, the peripheral circulation, and renal excretion plus infinite patience are the only measures which are available. If the block is of the non-depolarizing type administration of an anticholinesterase, such as 2·5 mg. of neostigmine methylsulphate preceded by 1 mg. of atropine, is usually followed by improvement in neuromuscular transmission.

Michael Kerr

619. **Why Thiopentone Injected into an Artery May Cause Gangrene**
J. H. BURN. *British Medical Journal* [*Brit. med. J.*] **2**, 414–416, Aug. 6, 1960. 12 refs.

This investigation was designed to determine whether the vasoconstriction of arteries which follows the arterial injection of thiopentone is due to the release of noradrenaline. At the Department of Pharmacology, Oxford University, rabbit aorta was suspended in a bath and was noted to contract when thiopentone was added to the solution in the bath. Injection of thiopentone into the central artery of the rabbit's ear caused a constriction of the ear vessels; this was shown not to be due to the *p*H of the injected solution. Cocaine, tolazoline, and reserpine were in turn added to the solution perfused through the ear. All 3 agents gave results consistent with the hypothesis that thiopentone causes arterial constriction by liberating noradrenaline from the artery walls. This theory is considered to be corroborated by the findings of Kinmonth and Shepherd (*Brit. med. J.*, 1959, **2**, 914; *Abstr. Wld Med.*, 1960, **27**, 506) that the area of gangrene produced in the ear by injection of thiopentone is greatly reduced by sympathectomy. Finally, the author demonstrated that the incidence of ulceration and gangrene produced in the mouse's tail by injection of thiopentone can be considerably reduced by previous treatment with reserpine.

Mark Swerdlow

620. **Drug Consumption during Thiopentone–Nitrous Oxide–Relaxant Anaesthesia: the Preparation and Interpretation of Time/Dose Curves**
M. KEÉRI-SZANTO. *British Journal of Anaesthesia* [*Brit. J. Anaesth.*] **32**, 415–423, Sept., 1960. 5 figs., 14 refs.

The thiopentone requirements of 101 subjects undergoing [at Notre Dame and Queen Mary Veterans' Hospitals, Montreal] a variety of surgical procedures lasting from 33 to 640 minutes were recorded and analyzed. It appears from the resulting equation that beyond the first hour of anaesthesia very little of the drug is translocated

while more than 90% is transformed. Transformation proceeds at least at double the rate previously assumed.

Thiopentone consumption is mainly determined by the active metabolic mass (measured most accurately as the body surface), the duration of anaesthesia and the plasma thiopentone level required to maintain anaesthesia in a particular subject.—[Author's summary.]

621. **Methohexital: a Short Acting Barbiturate**
J. COLEMAN and R. A. GREEN. *Anaesthesia* [*Anaesthesia*] **15**, 411–423, Oct., 1960. 3 figs., 15 refs.

The authors describe experience with methohexital for induction of anaesthesia in patients undergoing a wide variety of operations, dental extractions, and electric convulsion therapy. The drug was given intravenously as rapidly as possible, the average induction dosage being 7 mg. per 14 lb. (1·1 mg. per kg.) body weight; this consistently provided 2 minutes' sleep. Methohexital was considered to have twice the potency of thiopentone. For dental surgery a mixture of nitrous oxide and oxygen (85%:15%) was given as soon as the patient was asleep after induction of anaesthesia with methohexital; after 1½ to 3 minutes the percentage of oxygen was increased to 20 and extractions begun. In only 12 out of 373 dental patients was it necessary to supplement the nitrous oxide with another inhalation anaesthetic; 92% of the total number left the chair within 6 minutes of induction and 96% were fit to go home within half an hour. Vomiting occurred during recovery in only 5% and nausea in 14%.

[The number of extractions and duration of operation are not given.] *Mark Swerdlow*

622. **Clinical Experience with Chloroform Anesthesia**
M. F. POE and J. R. MAYFIELD. *Anesthesiology* [*Anesthesiology*] **21**, 508–511, Sept.–Oct., 1960. 14 refs.

The authors hold that chloroform as an anaesthetic agent has many advantages and may not be as dangerous as it is reputed to be. At the City of Memphis Hospitals (University of Tennessee) it was employed for 70 patients undergoing operations requiring a non-inflammable anaesthetic, but not if liver disease was known or suspected. In 29 cases the concentration of chloroform was 1% or less, in 10 it was 1·5% to 1·75%, and in only one case did it reach 2%. There were no serious complications. In 4 of the cases a change was made to some other anaesthetic. The chief disadvantages were hypotension and tachypnoea. Three deaths occurred, but none could be attributed to the anaesthesia.

The authors [wisely] recommend that in chloroform anaesthesia (1) the dangerous induction stage be carried out with some other drug and atropine should be given beforehand; (2) the maintenance concentration should be kept level at 0·5 to 1%, with no sudden increases, which are dangerous; (3) carbon dioxide should be thoroughly removed by maintaining adequate ventilation; and (4) the use of chloroform is contraindicated in patients with liver disease.

[The present abstracter cannot but deplore the current trend towards the reintroduction of chloroform anaesthesia. This anaesthetic agent has been the cause of many fatalities in the past and in the abstracter's view the problem of delayed chloroform poisoning is even to-day far from being solved, two deaths from hepatic necrosis having been reported from the Madison school as recently as 1956 (*Anesthesiology*, 1956, **17**, 792).]
W. Stanley Sykes

623. **Renal and Cardiovascular Effects of Halothane**
W. P. BLACKMORE, K. W. ERWIN, O. F. WIEGAND, and R. LIPSEY. *Anesthesiology* [*Anesthesiology*] **21**, 489–495, Sept.–Oct., 1960. 1 fig., 13 refs.

The renal and cardiovascular effects of halothane, which is a powerful, non-explosive, and non-irritant anaesthetic, were studied at the University of Texas Southwestern Medical School, Dallas. Induction was smoother than with ether, but hypotension with slowing of the heart and an increase in the respiratory rate occurred. There was a decrease in the urine flow, the glomerular filtration rate, and the renal plasma flow rate, with an increase in potassium excretion.

The authors conclude that there is a correlation between the cardiovascular and the renal effects of halothane and that the drug in sufficient concentration has a significant but reversible action on renal activity.
W. Stanley Sykes

624. **Skeletal Muscle, Esophageal and Rectal Temperatures in Man during General Anesthesia and Operation**
H. WOLLMAN and T. H. CANNARD. *Anesthesiology* [*Anesthesiology*] **21**, 476–481, Sept.–Oct., 1960. 9 refs.

A reduction in muscle temperature prolongs and intensifies the action of some relaxants; it has been suggested that prolonged apnoea in some cases may be related to this phenomenon. At the Hospital of the University of Pennsylvania, Philadelphia, the skeletal, oesophageal, and rectal temperatures were recorded by means of a tele-thermometer in 23 patients during operation, the average duration of which exceeded two hours. There was a decrease in temperature at all the sites, this decrease being most marked during thoracic operations.

In a discussion the authors state that heat gain in anaesthetized patients from a theatre temperature above 25° C. or from high humidity has been described by a number of workers, but their own findings suggest that heat loss is more common than has hitherto been recognized. Heat loss may be due to lessened heat production in curarized skeletal muscle, increased radiation from the skin, and evaporation of sweat, of cool liquids used in the preparation of the skin, and from exposed moist surfaces in the wound; [this last is especially important in the case of open thoracic incisions]. In thoracic operations the muscle temperatures may be reduced sufficiently to prolong and intensify depolarization blockade. It is suggested that rewarming of the patients may minimize this effect. *W. Stanley Sykes*

625. **Effects of Anesthesia upon the Heart.** [Review Article]
B. ETSTEN and T. H. LI. *American Journal of Cardiology* [*Amer. J. Cardiol.*] **6**, 706–715, Oct., 1960. 7 figs., bibliography.

Radiology

626. **Radioactive Strontium in Bone Disease.** (Le strontium radioactif en pathologie osseuse)
R. A. GUÉRIN and M. T. GUÉRIN. *Presse médicale* [*Presse méd.*] **68**, 1575–1576, Oct. 1, 1960. 11 refs.

Writing from the Institut National d'Hygiène, Paris, the authors state that among the 15 isotopes of strontium only ^{89}Sr and ^{85}Sr are suitable for clinical use. After discussing the physical properties of the known isotopes of strontium they describe a study of the value of ^{85}Sr in the diagnosis and treatment of diseases of bone, this isotope (half-life 63 days) being chosen because its emission of γ rays greatly facilitates detection and measurement.

Methods employing ^{85}Sr for the investigation of fractures are described. Also investigated were Paget's disease, bone metastases of carcinoma of the breast and prostate, myeloma, and osteitis, blood levels and urinary excretion of ^{85}Sr being measured. The fixation of ^{85}Sr in bones after irradiation has likewise been studied. Although diagnostic tests were performed on 34 patients, the therapeutic use of ^{85}Sr was attempted only once, in a case of myeloma, the patient receiving a total dose of 428 μc. This was followed by relief of pain, but not by radiological improvement.

The authors conclude that the diagnostic use of ^{85}Sr has no disadvantages and should be of considerable help. The isotope has no curative value, however, its only action being to relieve pain.

[The quantity used diagnostically is not stated, and radiation doses to bone and tissue have not been calculated.] *K. E. Halnan*

627. **Haematemesis and Melaena: Their Early Radiological Investigation**
G. N. CHANDLER, A. D. CAMERON, A. H. NUNN, and D. F. STREET. *Lancet* [*Lancet*] **2**, 507–510, Sept. 3, 1960. 5 figs., 17 refs.

The authors describe a simple bedside radiological investigation which they have found to be of diagnostic value in the acute stages of bleeding in cases of haematemesis and melaena. Of 183 such cases admitted to the Central Middlesex Hospital, London, in the year from November, 1958, 33 were excluded for various reasons, and the remaining 150 were investigated by barium-meal examination in the ward as soon after their admission as possible. A final diagnosis was made at a second barium-meal examination in the x-ray department after haemorrhage had ceased, or at operation or necropsy. Of 16 patients whose bleeding was considered at the first radiological examination to have been due to chronic gastric ulcer, this diagnosis was proved correct in 12, a diagnostic accuracy of 75%. The presence of a chronic duodenal ulcer was accurately forecast in 52 out of 54 patients (96% accuracy of diagnosis). In 2 patients with oesophageal varices and 2 with carcinoma of the stomach a correct diagnosis was made by the early method. Of 72 patients whose barium-meal examination was negative, 53 were thought to have bled from acute ulcers. The over-all accuracy of the method was 83%, and the authors consider it to be of great help in deciding whether to treat the patient conservatively or by surgical means. *I. McLean Baird*

628. **Two Vascular Grooves of the External Table of the Skull Which Simulate Fractures.** [In English]
H. SCHUNK and Y. MARUYAMA. *Acta radiologica* [*Acta radiol. (Stockh.)*] **54**, 186–194, Sept., 1960. 12 figs., 5 refs.

Two grooves of the skull which are frequently mistaken for fractures have been demonstrated to be vascular grooves of the external table of the skull, due to the middle temporal artery in the temporo-parietal region, and to the supraorbital artery in the frontal region.—[Authors' summary.]

RADIOTHERAPY

629. **Inoperable Cancer of the Bronchus Treated by Megavoltage X-ray Therapy**
R. MORRISON and T. J. DEELEY. *Lancet* [*Lancet*] **2**, 618–620, Sept. 17, 1960. 2 figs., 11 refs.

In a previous paper (*Lancet*, 1957, **2**, 907; *Abstr. Wld Med.*, 1958, **23**, 390) the authors reported the preliminary results of megavoltage (MeV.) x-ray therapy of inoperable carcinoma of the bronchus in 199 patients at the Hammersmith Hospital, London. They now report the progress of the same group of patients and of an additional 78 treated since 1957. Of the 277 patients only 20 were females. Histologically, squamous-celled carcinomata were present in 49%, anaplastic or oat-celled tumours in 28%, and adenocarcinomata in 3%. On the basis of the clinical and radiological findings or the appearances at bronchoscopy or thoracotomy the patients were divided into two groups—those with and those without mediastinal lymph-node metastases. Treatment was given on the 8 MeV. linear accelerator, and aimed at 4,500 rads in 4 weeks by daily exposures, but when the volume of tissue to be irradiated was very large the dose was reduced to 3,500 rads. The zone of tumour opacity with a 2-cm. margin and the mediastinal lymph-node areas were irradiated.

Haemoptysis was arrested in 94% of the cases and dyspnoea, pain, and cough in 75%. The survival curve flattened after 3 years, but 6% of the patients lived 5 years or longer. The 3-year survival rate of patients with squamous-celled tumours was 8·9%, and of those with anaplastic tumours it was 1·5%; 10% of patients with squamous-celled carcinoma without lymph-node involvement lived 3 years. The prognosis was significantly

better in patients with upper- and middle-lobe tumours than in those with lower-lobe tumours. The authors point out that because of diminished radiation reactions with MeV. it was possible to treat larger tumours than with 240 kV. Of 176 patients given 240-kV. therapy, 2% survived 5 years, but the results of the two methods differed little in patients with anaplastic tumours. In the authors' view MeV. x-ray therapy is indicated in patients with inoperable disease who are not severely debilitated and who have squamous-celled tumours without evidence of spread outside the chest. In a number of cases of lung cancer the tumour at necropsy is still confined to the chest. When treatment is started, 2 out of every 3 patients with squamous-celled lesions and one out of 3 with anaplastic lesions have no evidence of tumour spread beyond the primary site. In about half the patients, therefore, the disease can be cured by effective local treatment. "With high-energy radiation a relatively greater tumour-to-normal-tissue dose ratio is possible than with 240 kV. x-rays, permitting a slightly higher tumour dose to be given with less damage to the normal tissues." *I. G. Williams*

630. **Prevention of Bleeding in Esophageal Varices by X-ray Radiation: Pilot Study and Case Report**
R. D. EICHHORN and O. LEITE. *American Journal of Gastroenterology* [*Amer. J. Gastroent.*] **34**, 266–274, Sept., 1960. 18 refs.

An important factor in the aetiology of bleeding from oesophageal varices is peptic digestion of a weakened oesophageal mucosa and venous wall. The authors of this paper from Baylor University College of Medicine, Houston, Texas, review the literature on the use of x-irradiation to reduce the secretory activity of the stomach in the treatment of peptic ulcer. It reduces gastric secretion by over 50% and leads to healing of ulcers. They conclude that x-irradiation is justified in cases of oesophageal bleeding in which surgery is contraindicated or refused or other treatment has failed.

One case of portal hypertension treated by x-irradiation is described in detail, but the patient died from intercurrent disease before sufficient time had elapsed to assess the results. The technical factors were: 2 MeV. (Van de Graff), single anterior field 15 cm. × 8 cm., minimum gastric mucosal dose of 2,000 r. (10 × 200 r. daily), location by barium contrast fluoroscopy, and confirmation by a radiograph taken under treatment conditions. The authors consider the method worthy of extended trial not only in cases of oesophageal varices but also in cases of hiatal hernia and peptic oesophagitis. *J. Walter*

631. **Primary Neoplasms of the Liver. Results of Radiation Therapy**
R. PHILLIPS and K. MURIKAMI. *Cancer* [*Cancer (Philad.)*] **13**, 714–720, July–Aug., 1960. 8 refs.

Since 1926, in the records of Memorial Hospital [for Cancer and Allied Diseases, New York], there have been only 32 cases of primary neoplasms of the liver treated by radiation therapy. Yet in national death rate reports, primary cancer of the liver is as frequent as cancer of the esophagus or cancer of the ovary, and the possibilities of radiation therapy in its management seem to have been overlooked.

The results of radiation therapy in 26 cases of hepatocellular carcinoma are analyzed. In 4 cases the tumor dose was less than 2,000 r and was ineffective. In 22 cases the tumour dose was more than 2,000 r (average 2,956 r in an over-all time of 23 days); there was marked tumor regression in 9 cases and measurable regression in a further 5 cases; there was excellent symptomatic improvement in 11 cases and some improvement in 5 cases; the duration of life after radiation therapy averaged 12 months, which is 3 times the average total duration generally reported for this disease. There are reasons, however, for supposing that these cases in which radiation was used are not typical of the disease as generally reported for the following reasons: the average duration of symptoms before diagnosis and irradiation was 12 months, there were equal numbers of male and female patients, and 18 of the 26 patients were less than 45 years of age. On the other hand, the results are in line with those previously reported for metastatic liver cancer, and the structure of hepatocellular carcinoma would make it at least as radiosensitive as carcinomatous metastases in the liver.—[Authors' summary.]

632. **Carcinoma of the Prostate. Treatment by Interstitial Irradiation with Radioactive Gold. Experimental and Clinical Studies**
G. J. BULKLEY and V. J. O'CONNOR. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **174**, 252–256, Sept. 17, 1960. 5 figs., 9 refs.

It has been shown that following intraprostatic injection of radioactive colloidal gold (^{198}Au) in dogs about 10% of the isotope injected acts directly on the prostate gland. Assuming a similar distribution in human beings, the authors at the Wesley Memorial and the Veterans Administration Research Hospitals, Chicago, treated 42 patients with carcinoma of the prostate by intraprostatic injections of ^{198}Au. All the patients received oestrogen therapy as well and about half had undergone orchidectomy. Tumour destruction was patchy and incomplete even when the dosage was high and the injections were repeated. Over-all survival was not increased. Assessment of palliation was chiefly objective (palpation). Of the 42 patients 20 died (3 of these had had temporary palliation); 20 were still alive and 2 were lost to follow-up. Improvement was noted in 17 of the 20 survivors, with complete arrest of tumour growth in 7. It is concluded that only in rare, isolated instances is palliation by this method worth while. The best results were obtained in patients who had a small localized mass in the prostate. The method can suitably be used in patients who refuse radical surgery or in whom surgery is contraindicated and in those with small localized areas of carcinoma. *P. Banerjee*

633. **A Technique for Continuous Intra-arterial Infusion**
H. HORWITZ. *British Journal of Radiology* [*Brit. J. Radiol.*] **33**, 679–683, Nov., 1960. 3 figs., 11 refs.